THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—39TH YEAR SYDNEY, SATURDAY, DECEMBER 13, 1952 No. 24

Table of Contents.

TUBERCULOSIS IN CHILDHOOD, AS DISCLOSED OR CONFIRMED BY CULTIVATION OF MYCOBACTERIUM TUBERCULOSIS FROM GASTRIC CONTENT.

By REGINALD WEBSTER,
Children's Hospital, Melbourne.

THE object of the ensuing report and discussion is not to reiterate the value of cultural methods applied to gastric content in the diagnosis of tuberculosis in childhood, although such an effect cannot fail to emerge incidentally. Indeed, if I felt that I could discount the utility of the procedure I would be tempted to make the effort, in the hope of effecting some reduction in the volume of laboratory work for which it is responsible. Rather is it my intention to discuss some general principles as they are illustrated by 162 children from whose gastric mucus I have cultivated tubercle bacilli, and consider problems in diagnosis, immunology, pathogenesis, and morbid anatomy presented by sundry individual patients, and groups of children arranged on a basis of their dominant clinical features.

TUBERCULIN SENSITIVITY.

Among the 162 children in whom the diagnosis of tuberculosis was established by the cultivation of *Mycobacterium tuberculosis* from the gastric content were eight who exhibited no reaction to the intracutaneous injection of 0·1 millilitre of a 1 in 1000 dilution of old tuberculin. With one exception all the patients in whom tuberculin sensitivity was depressed to such degree were extremely ill, the failure to respond to the tuberculin test bespeaking the loss of sensitivity which portends the fatal issue in rapidly advancing tuberculosis. Diminution of sensitivity in the moribund may be carried to the point of abolition, and is attributable to the elimination by exhaustion of the antibody participant in the reaction of hypersensitivity, by an overwhelming access of antigen in the form of endogenous tuberculo-protein; excessive output of antigen may attend the rapid multiplication of the countless microorganisms involved in miliary tuberculosis, or an avalanche may ensue on such a disaster as the discharge into the blood stream of the caseous content of a necrotic focus, possibly rich in tubercle bacilli, but at all events supercharged with tuberculo-protein.

The exception in this group of children in whom failure to respond to the routine Mantoux test was referable to desensitization by exhaustion of antibody was a girl, aged eight years (number 131), the second of five patients whom streptomycin therapy enabled to achieve apparently flawless recovery from meningeal tuberculosis as recorded by B. A. Neal and S. W. Williams (1951). In their report on the results attending treatment by streptomycin of 29 children suffering from bacteriologically confirmed tuberculous meningitis, the authors named mentioned that four of the patients exhibited no reaction to the routine intracutaneous (Mantoux) tuberculin test, but that in one child the capacity to react to tuberculin was regained as clinical improvement progressed. Such an observation suggests that just as temporary suppression of tuberculin sensitivity may follow the onset of tuberculous pleurisy, initiated by the irruption of the contents of a caseous primary focus or hilar lymph node into the pleural cavity (Rich, 1946), reactivity to tuberculin may be greatly reduced or even abolished, with the supervention of meningeal tuberculosis on the disintegration of a caseous focus impinging on the subarachnoid space.

In general terms it may be stated that the hypersensitivity to tuberculo-protein induced by infection with

Mycobacterium tuberculosis has not the fixed and immutable quality attributed to the law of the Medes and Persians, "which altereth not", but is subject to fluctuations. Even during the course of progressive tuberculosis cutaneous reactivity may wax and wane, and a temporary eclipse is not uncommon. A lowering of cutaneous sensitivity to tuberculin has frequently been observed in intercurrent infections, particularly measles, and in dehydrated and cachectic states in which the reactivity of the cutaneous vessels to irritants in general is impaired. The diminution or abeyance of the inflammatory response to the injection of tuberculin under such circumstances is less a specific desensitization to tuberculo-protein than a non-specific modification of the reaction potential of the skin, or, more accurately, the cutaneous capillary blood vessels.

There would seem to be little reason to doubt that a true desensitization with respect to tuberculo-protein underlies the fading and eventual disappearance of reaction to tuberculin after the healing or arrest of a tuberculous process. The maintenance of the hypersensitive state in tuberculous infection is dependent upon the stimulus to antibody formation provided by the absorption of a frequently replenished supply of the provocative antigen, elaborated by tubercle bacilli in action. With healing or arrest of the lesion, and the extinction, or perhaps suspension, of animation and cessation of multiplication of the bacilli, the trickle of sensitizing antigen dries at its source and the tension of the hypersensitive state is resolved.

An informative study which demonstrated the disappearance of specific skin hypersensitivity in tuberculosis as the result of successful resistance of infection, is that of M. Paretzky (1936), whose report is based on the examination of 80 persons in whom a swing to "negative" in cutaneous reactivity to tuberculin had been noted; 68 of the patients were children, of ages ranging from infancy to fourteen years. All had positive tuberculin records or other acceptable evidence of preexisting tuberculosis. In 33 of the 80 patients selected for investigation the cutaneous reaction to tuberculin receded to a point at which it could not be elicited by the intracutaneous injection of 10·0 milligrammes of tuberculo-protein, and remained so suppressed throughout the period of observation and retesting. The time during which individual patients were under observation varied from a minimum of one year and seventeen days to a maximum of five years five months and six days. In 17 patients cutaneous reactivity to tuberculin was reestablished, but for various reasons retesting could not be satisfactorily pursued in the remainder. The author emphasized that the majority of the reactors to tuberculo-protein chosen for retesting had acquired infection by close and intimate contact within the narrow confines of the immediate family, from tuberculosis sufferers likely to be in no small degree infective.

The demonstration of reduction of sensitivity to tuberculin to a degree which rendered it undetectable by intracutaneous injection of the mammoth dose of 10·0 milligrammes of tuberculo-protein would seem to establish, in a manner which should convince the most sceptical, that the hypersensitive state induced by primary tuberculous infection, so far from being inevitably a life sentence, may be terminated by the withdrawal of antigenic stimulus implicit in the healing or arrest of the lesion.

References.

Neal, B. A., and Williams, S. W. (1951), "Meningeal Tuberculosis in Children: A Review of Forty Patients", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 676.

Paretzky, M. (1936), "The Disappearance of Specific Skin Hypersensitiveness in Tuberculosis: A Report Based on 80 Cases", *The American Review of Tuberculosis*, Volume XXXIII, page 370.

Rich, A. R. (1946), "The Pathogenesis of Tuberculosis", Charles C. Thomas, Springfield, Illinois, page 369.

HOUSEHOLD INFECTION.

The problem of the tuberculous child is the problem of the tuberculous adult, for without doubt the overriding factor in the propagation of tuberculosis among children is the presence within the home of an adult subject of so-called "open" tuberculosis. Bovine sources of tuberculous infection, though not to be underrated, recede into relative insignificance when considered against the prolific and often unwitting human agencies. *Mycobacterium tuberculosis*, as cultivated from the gastric content of the 162 children under review, was invariably of the human type, and it was ascertained that 90 of the young patients came from homes in which they had lived in the close contact inseparable from family life with a phthisical mother (43), father (35), brother or sister (6), or lodger (6). The less intimate contact with tuberculous relatives or with neighbours who were frequent visitors was noted in 25 instances. A clean sheet with respect to tuberculosis in the child's family was entered for 37 of the bacteriologically identified tuberculous children, and for the remaining ten the case records lack information in this particular.

No good purpose will be served by labouring the truism that children exposed to domiciliary infection by *Mycobacterium tuberculosis* are subjected to a hazard which, by comparison with that obtaining for their contemporaries of healthy stock and limited to casual contact outside the home, is in high degree exalted and too often insurmountable. Many careful and well-documented studies have established the fact that children deriving from tuberculous households exhibit a much higher incidence of tuberculosis mortality and morbidity than do those whose immediate environment is free from the acid-fast bacillus which "sheds its substance on the floating air". But it may be of interest to examine the problems in pathogenesis and immunology inherent in frequently repeated infections with tubercle bacilli, and to search for some explanation of the fact that primary foci, as observed in routine autopsy work on children who have died of progressive tuberculosis, are much more commonly single than multiple, even when the subject of the autopsy has been a member of a household in which he might reasonably be presumed to have been inoculated with tubercle bacilli by inhalation on many occasions. A single pulmonary focus, participating in a primary complex, is the usual but not invariable finding, as bears witness a specimen illustrative of a duocentric primary focus which holds a place in the museum of pathology of the Children's Hospital.

In a report of his studies of the morbid anatomy of primary tuberculous infection of the lung, as exhibited by 35 children in whom tuberculosis was the cause of death, Terplan (1940), who for eleven years had as his mentor that foremost of all exponents of the primary complex, Anton Ghon, recorded two instances of dual primary foci; in 23 autopsies in which tuberculosis was but an incidental finding, there occurred three examples of a double primary focus, by which is to be understood two foci in a calcified state, with calcified lymph nodes regional to each.

The lesion of entry of the tubercle bacillus when it effects a lodgement in the lung may be very small, and I have on more than one occasion found the primary focus difficult to locate when its presence was clearly indicated by the caseous condition of the hilar lymph nodes. In the pursuit of the daily round and common task in the post-mortem room, however, I have met with multiple primary foci on few and widely separated occasions.

Infection Immunity.

A feasible explanation of the fact that only one primary focus of macroscopic dimensions should appear as a rule in the lung of a child who has sustained repeated infections from a domiciliary source, would seem to be found in the conception of infection immunity—a theory which suggests that once infection with a bacterial parasite is established the host will be immune to reinfection with that particular bacterium until such time as his tissues are freed from it altogether, when susceptibility will return.

The doctrine of infection immunity rests largely upon results which have been obtained in the study of experimental syphilis in the rabbit. In this infection it is possible, by administering an adequate dose of "Neosalvarsan" or other appropriate arsenical drug, to cure the initial infection and to observe the effect of so doing on the resistance of the rabbit to reinfection. Brown and Pearce

(1921) infected a number of rabbits and treated some of them with arsphenamine shortly after the development of the primary chancre. Five days later these rabbits were injected with the same strain of *Treponema pallidum*. Most of the treated animals developed chancres, while the untreated animals did not. Topley and Wilson (1946) summarize the conclusions to be drawn from the findings of the several investigators in this field. In experimental syphilis in the rabbit immunity to reinfection seems to be established within a short time after the appearance of the initial lesion. At this stage the maintenance of immunity depends on the maintenance of infection; complete chemotherapeutic cure is followed by a return of susceptibility. But after a longer period of infection a partial immunity is established which may persist after complete chemotherapeutic cure; and after still longer periods of infection a complete immunity may be established and remain independent of the persistence of infection.

A closely analogous situation may be discerned in experimental tuberculosis. That the induction of tuberculous infection in the guinea-pig evokes a notable degree of resistance on the part of the animal to a second inoculation with tubercle bacilli is the essence of the classical Koch phenomenon, in which it will be recalled that, provided the second inoculation of tubercle bacilli is withheld until after the development of the lesion initiated by the first, so far from inducing a second caseating nodule with involvement of the regional lymph nodes, the further injection of tubercle bacilli excites a small necrotic lesion which heals promptly, the bacilli responsible for it not reaching the lymph nodes in relation to the site.

The pioneer observation of Robert Koch has been amplified by various investigators, among whom are Debre and Bonnet (1922), whose experiments were designed to determine the effect of the time interval elapsing between the initial injection of the guinea-pig with 0·1 milligramme of tubercle bacilli and the subsequent injection of the same dosage. It was found that with the dosage employed Koch's phenomenon did not exhibit its decisive and dramatic quality until about six weeks after the first injection, and of major importance was the demonstration that clinically evident superinfection of a tuberculous guinea-pig was impracticable after the appearance of the local caseating nodule. Before the local abscess appeared the guinea-pig reacted to a fresh infection just as a normal animal; but once the local lesion due to the first injection had developed—generally in about eight to ten days—the lesions induced by subsequent injections became less and less, as the time intervals in relation to the first were drawn further and further, until after six weeks the freshly injected microorganisms were summarily cast off by an acute reaction, the tissue damage incidental to which was soon repaired.

In the study of experimental syphilis it has been shown that it is possible to produce in the ape a series of chancres, so long as the following injections are made before the appearance of the primary chancre; once the primary sore has materialized, further inoculation of syphilitic material fails to produce a chancre.

The concept of infection immunity is thus seen to be applicable in both tuberculosis and syphilis. So long as infection persists, and so long as the respective infecting microorganisms, *Mycobacterium tuberculosis* and *Treponema pallidum*, are present in the tissues, the infected animal is relatively resistant to further infection. It is possible for a patient to develop two chancres, provided the second infection occurs before the appearance of the first and primary sore; but once a chancre has developed, further infections almost invariably fail to give rise to such a lesion. Similarly, in Debre and Bonnet's extended experiments on the Koch phenomenon, it was found that when the second injection of tubercle bacilli was made within eight to ten days of the first, the respective lesions induced in the guinea-pig were identical; as the intervening time was increased the second lesion progressively diminished in size and severity until eventually it could not be induced.

Fallacy, of course, is prone to attend the application to the human subject of conclusions based on observations in the guinea-pig, notoriously destitute of native resistance, but civilized man's more fortunate endowment in this respect should lend the ensuing argument greater force. One might draw a parallel between the experimental conditions which have allowed the exhibition of a state of infection immunity by the guinea-pig, and the environment of a child who runs the gauntlet of frequently repeated infections with tubercle bacilli from a phthisical relative in the home. If the analogy be allowed it would seem logical to suggest that the fact that primary tuberculous foci in the lung of such a child are more often single than multiple is no matter for surprise.

If a degree of acquired resistance, becoming operative after the lapse of the short period of eight or ten days required for the development of the initial lesion, at first in feeble fashion, but as week succeeds week in progressively decisive manner, can be induced in the very susceptible guinea-pig, should not the child, aided thereto by a measure of native resistance which the guinea-pig lacks, be capable of dealing with the later of successive exogenous inoculations at least as effectively as the experimental animal? The child has a further advantage over the guinea-pig of the Koch phenomenon in that the inoculating doses he is likely to incur from an infective member of his family circle convey many less tubercle bacilli than are represented by 0·1 milligramme of tubercle bacillus culture, the inoculum which workers following Koch have employed for the further study and confirmation of his historic experiment.

The logical implication of the conception of infection immunity is that pulmonary tuberculosis supervening in the later life of an individual who has succeeded in arresting, but not completely eradicating, a primary infection is of necessity endogenous, a view promulgated by Ronzoni (1927) and formulated in dogmatic terms by Fishberg (1932); in the van of those who believe that the so-called "adult" type of pulmonary tuberculosis is with few exceptions to be attributed to exogenous reinfection is Opie (1933), and the controversy cannot yet be said to be resolved.

Reaction to Multiple Inoculations.

Should effective inoculating doses of tubercle bacilli be implanted in the lungs in serial fashion, the character of the lesions induced will be determined by the intervals elapsing between the first to establish a focus of tuberculous disease and subsequent infections. Successive inoculations by inhalation occurring in the vulnerable period preceding the development of the initial lesion and the concomitant assertion of reactive resistance and hypersensitivity may be expected to exhibit their effects in lesions identical with the first, thereby giving rise to multiple primary foci. As the interval between the first and later inoculations lengthens, and the development of the hypersensitive and resistant state gains momentum, the capacity of the later arriving detachments of tubercle bacilli to induce a disease focus of macroscopic dimensions will become progressively less and less, until finally they are impotent in this respect. It does not follow that the first focus and any that may postdate it by a brief interval will recede, although they frequently do so, as the bacilli entrenched therein have been permitted time to multiply in the period required for the gearing of the defensive mechanism; after all, the guinea-pig in the Koch phenomenon is destined to die from generalized tuberculosis supervening on the relentless advance of the initial lesion, although within a few weeks the animal is refractory to attempts at superinfection. Aided by a degree of native resistance to which the guinea-pig cannot pretend, the child exposed to frequently repeated domiciliary tuberculous infection should the more rapidly acquire the capacity to reject detachments of tubercle bacilli following in the wake of the first to initiate a focus of disease, and it is submitted that herein lies the explanation of the post-mortem observation that in children dying of tuberculous disease, as in those in whom a tuberculous primary complex is but incidental to the cause of death, primary foci are in the majority of instances single rather than multiple.

It is possible that conclusions as to the relative rarity of multiple primary foci based on gross morbid anatomy may

be fallacious. Small tuberculous lesions may be only too easily overlooked, and it may well be that those rendered abortive by the development of resistance and concomitant hypersensitivity may be represented by tiny scars, the presence or significance of which may elude the most alert and painstaking morbid anatomist. For the detection of small primary tuberculous foci in the lung the clinician has learned to put not his trust in radiology, but perhaps primary tuberculous foci would be found to be accompanied by recessive subsidiaries more frequently than is ordinarily apparent, by routine X-ray examination of the lungs excised *post mortem*.

Effect of Repeated Infections on Resistance.

The question whether frequently repeated infections with tubercle bacilli, in the comparatively small numbers which may be inhaled on any single occasion from a human source, operate to depress resistance, or serve as a stimulus to the maintenance of a high titre of defensive antibodies, is one on which opposing views have not yet been reconciled. The principles of immunology, as they prevail in other infections, suggest that the mechanism which rejects predatory tubercle bacilli, seeking a lodgement after the establishment of the primary focus in the lung, and limits such focus to one in the majority of instances of household infection, should be sustained and even exalted by this exercise. Should this be so, the deplorable consequences of household contact in the propagation of tuberculosis would seem to be mitigated by a small measure of compensation, and communications embodying the findings in an inquiry directed towards the elucidation of this point are those of S. Lyle Cummins (1926, 1935).

In his first report (1926) the late Professor Cummins presented the results of a well-organized investigation the object of which was to assess the clinical course of tuberculosis in persons known to have contracted the disease by familial contact, as compared with that in patients from whom no history of contact could be elicited. From a table based on analysis of the records of 3346 subjects of tuberculosis, it appears that amongst patients whose disease was referable to household contact, there existed in every clinical group analysed a greater proportion of relatively favourable types than obtained for corresponding groups in the total of individuals for whom no familial contact could be determined. In a later communication (1935), when the number of deaths over a period of from eight to ten years was known, the same author compared the mortality amongst the clinical groups with no known contact and the death rates in the family contact groups. In a series of 492 patients, known to be familial "contacts", in whom pulmonary tuberculosis was in an acute and initial stage when they first came under observation, the survival rate was 41%, as against 33% of 863 persons in similar clinical state who had no knowledge of contact with tuberculosis. Similarly, in patients classified clinically as "chronic recrudescent" types, the survival rate in 231 members of tuberculous families was 46%, while that of 366 of negative family history was 41%. The data in these studies were collected largely from adults, but a similar investigation relating specifically to children was that of Eliasberg (1919), from whose report it appeared that the progress of the disease was more chronic, and the mortality 37% lower, in children who contracted progressive tuberculosis from a source of infection within the home than in those infected by casual contact with an outside source.

No attempt will be made to draw any conclusion from the statistically small series of 162 children under present review by virtue of the fact that the basis of diagnosis was the cultivation of *Mycobacterium tuberculosis* from the gastric content. Actually those children whose tuberculosis derived from a familial source fared worse than those who contracted infection by casual contact without the home, 55·5% of the former group incurring progressive disease or death, and 35·5% a comparable measure of affliction in the latter group. The issue is far from determined and for each report which seems to confirm the opinion that repeated intrafamilial infections operate to enhance the subject's acquired resistance, there may be found another of the nature of a counterblast.

Interesting observations relating to the problem of the infection of children of tuberculous households are those of Miriam Brailey (1940), who studied the sensitivity to tuberculin of 793 children, of a maximum age of fifteen years, who had lived for varying periods of time in contact with an adult known to be eliminating tubercle bacilli in the sputum. As was to be expected, the proportion of reactors to tuberculin rose steadily with lengthening periods of exposure, from 37% in the group of less than one month to 76% in that of six to twelve months. Of children subjected to more than one year of household contact with an adult demonstrably infective, 175 of 205 (or 85·4%) reacted to tuberculin. The tenor of the results might perhaps have been anticipated, but it is of some interest to note that 24% of children domiciled with an adult, the order of whose infectivity was certainly not low, for six to twelve months, and 15% of those similarly situated for more than twelve months, escaped infection as judged by their failure to react to 1·0 milligramme of tuberculin. Such an evasion rate in the families of low social status to which Brailey's figures related led her to suggest that in the better living conditions and superior hygiene of those more fortunately situated economically, contact infection was by no means inevitable.

References.

Brailey, M. (1940), "A Study of Tuberculous Infection and Mortality in the Children of Tuberculous Households", *The American Journal of Hygiene*, Volume XXXI, page 1.

Brown, W. H., and Pearce, L. (1921), "Superinfection in Experimental Syphilis following the Administration of Subcurative Doses of Arsphenamine or Neoarsphenamine", *The Journal of Experimental Medicine*, Volume XXXIII, page 553.

Cummins, S. L. (1926), "The Significance of Variations in Clinical Type in Pulmonary Tuberculosis", *Tubercle*, Volume VII, page 375.

——— (1935), "Contact with Infection in Tuberculosis", *Canadian Public Health Journal*, Volume XXVI, page 1.

Debre, R., and Bonnet, H. (1922), cited by Topley and Wilson, Third Edition, Volume II, page 1326.

Eliasberg, H. (1919), cited by A. R. Rich, "The Pathogenesis of Tuberculosis", 1946, page 677.

Fishberg, M. (1932), "Pulmonary Tuberculosis", Lea and Febiger, Philadelphia.

Opie, E. L. (1933), "Recognition and Control of Tuberculosis in Childhood", *The American Journal of Public Health*, Volume XXIII, page 305.

Ronzoni, G. (1927), "The Communicability of Tuberculosis in Adults", *The American Review of Tuberculosis*, Volume XV, page 1.

Terplan, K. (1940), "Anatomical Studies on Human Tuberculosis", *The American Review of Tuberculosis* (Supplement), Volume XLII.

Topley, W. W. C., and Wilson, G. S. (1946), "The Principles of Bacteriology and Immunity", Third Edition, Edward Arnold and Company, London, page 1166.

Tuberculous Rheumatism.

The cultivation of *Mycobacterium tuberculosis* from the gastric content proved of particular interest in respect of five children (numbers 8, 26, 59, 76, 86), each of whom, largely as the result of the emphasis laid on joint pains in the clinical story, was admitted to the Children's Hospital as suffering from rheumatic fever. All reacted to the intracutaneous tuberculin test, and four of the five exhibited that symptom complex of fever, malaise, pains in the joints, and painful nodular cutaneous eruption connoted by the term *erythema nodosum*. The absence of redness, swelling and pain on movement of any joint noted during the stay in hospital of three of these children, and the lack of signs of cardiac involvement, suggested that the joint pains of which the young patients complained were of the nature of those allotted a place in the accepted syndrome of *erythema nodosum*, and final diagnosis was deferred pending bacteriological examination of the gastric content directed towards the detection of *Mycobacterium tuberculosis*. With regard to the fourth and fifth of the children admitted to hospital as suffering from acute rheumatism, the degree of probability attaching to such provisional diagnosis may be assessed from the following summaries of their clinical records, as may also be estimated the extent to which they conformed to the clinical entity "tuberculous rheumatism".

Bruce J. (number 59), aged three and a half years, was admitted to the Children's Hospital under a provisional diagnosis of rheumatic fever on December 4, 1944. Ten days prior to admission the child had complained of a sore throat and pain in the legs, upon which he based a refusal to walk. Nine days later the left ankle became sore; on the following day he would not use his left wrist, and protested that the joint was painful when touched. The child's temperature was found to be 103° F., his left wrist joint was slightly swollen and movement of the joint appeared to cause pain; no swelling or tenderness was apparent in any other joint. The diagnosis of rheumatic fever was accepted and seemed to gain support from the fact that a systolic bruit became audible in the mitral area. The child remained relatively well until the onset of whooping-cough on January 4, 1945.

An unequivocal reaction on the part of the little boy to the intracutaneous (Mantoux) tuberculin test, performed as a matter of routine, led to a radiograph of the chest, the report on which, dated January 18, 1945, passed the lungs as clear, but noted the presence of an enlarged cardiac shadow. Revision of the diagnosis of rheumatic fever was compelled by the cultivation of *Mycobacterium tuberculosis* from a specimen of gastric content withdrawn on January 26, 1945, a finding which suggested very strongly that an alternative and at least equally probable conception of the child's illness was primary tuberculous infection, with which rheumatic features, though occurring uncommonly, have become identified.

The fifth patient (Joan F., number 86), a girl, aged twelve years, whom a provisional diagnosis of rheumatic fever gained admission to the Children's Hospital, presented on August 16, 1946. An eruption certified as that of *erythema nodosum* by her family physician had appeared eleven weeks earlier, and in the interval the girl had suffered pains in the legs, which later extended to the arms and forearms, and with which was associated tenderness of the muscles of the limbs. Courses of treatment by sodium salicylate and sulphadiazine had effected no improvement, and much was made of the fact that the patient had sweated profusely during her illness.

Physical examination established that the muscles of the upper and lower limbs were hypotonic and tender, but the tenderness was not conspicuously periarticular, and the larger joints exhibited no inflammatory swelling. Foot-drop was noted, as also a suggestion of fusiform shape of the interphalangeal joints. The skin was sticky and exhaled a sudaminous odour. The treatment instituted was based on a diagnosis of subacute rheumatism.

Inquiry elicited a history of frequent contact with a companion's father, who had died of pulmonary tuberculosis. Reaction to the intradermal tuberculin test was violent and progressed to vesiculation. A slight degree of enlargement of the hilar lymph nodes on the right side was noted in the thoracic radiograph, in which no calcification or other pathological process in the parenchyma of the lung was apparent. *Mycobacterium tuberculosis* was cultivated from a specimen of gastric content of August 21, 1946.

In the two weeks following the girl's admission to hospital the pains in her limbs ameliorated to a great extent, and muscular power improved to a degree which permitted almost full range of movement. She continued to perspire freely, but at no stage exhibited any physical signs of cardiac affection.

The recovery of *Mycobacterium tuberculosis* from the gastric content of this patient resolved a difficulty in diagnosis. The pain, which had been the dominant feature throughout, was of the nature of myalgia rather than that occasioned by arthritis; further, the joints displayed no objective signs of arthritis, and no cardiac affection could be brought into evidence. The violent reaction to the intradermal tuberculin test, recent *erythema nodosum*, radiographic evidence of enlargement of the hilar lymph nodes, and cultivation of *Mycobacterium tuberculosis* from the gastric content were the positive factors which determined the final diagnosis as tuberculous rheumatism rather than rheumatic fever.

The simulation of rheumatism in its several manifestations by tuberculous patients in the phase of primary infection has attracted most attention in France, whence has emanated a book "*Le rheumatisme tuberculeux*", by A. Poncet and R. Le Riche (1909). Recorded observations on the part of British workers seem to be limited to those of Leonard Findlay (1920) and Wilfrid Sheldon (1946). In their book on the subject (1909) Poncet and Le Riche distinguish "primary" and "secondary" types of tuberculous rheumatism, according as the arthritis or myalgia precedes or follows the development of features which lead ultimately to the diagnosis of tuberculosis. They describe three main clinical forms of tuberculous rheumatism: (1) arthralgia, (2) acute arthritis, with which may be associated inflammation of serous membranes, especially pericarditis, and (3) chronic rheumatism, or rheumatoid arthritis.

In reporting details of six children whom he presented as illustrative of the clinical syndrome of "tuberculous rheumatism", Sheldon (1946) included one example of arthralgia, four of acute polyarthritis which closely reproduced the familiar clinical picture of rheumatic fever, not excepting the occurrence of pericarditis in one patient, and one of arthritis of "rheumatoid" type. Findlay's communication was based on the case records of three children whom he regarded as subjects of tuberculous rheumatism. He emphasized that in its more acute manifestations the condition might resemble ordinary rheumatic fever to the extent that fever, pain and swelling flitting from joint to joint and associated pericarditis masked the correct diagnosis until the onset of some frankly tuberculous development.

In retrospect and with the advantage gained by opportunities for accurate assessment of physical signs provided by the stay in hospital of the two children whose illness I have presented as tuberculous rheumatism, there are seen to be certain anomalies which render the provisional diagnosis of rheumatic fever questionable. In the case of the boy Bruce J. (number 59) objective signs of arthritis were apparent in the left wrist joint only, though there had been complaint of pain in the legs and soreness of the left ankle. The dominating features in the illness of the girl Joan F. (number 86) were severe and protracted myalgia, profuse sweating and antecedent *erythema nodosum*. Obstacles to the unreserved acceptance of the diagnosis of rheumatic fever were the absence of inflammatory swelling of the joints proper and the lack of signs of cardiac involvement. It will perhaps be agreed, however, that the general aspect of both children was sufficiently "rheumatic" to suggest rheumatism as a first diagnosis, and that failing the recovery of *Mycobacterium tuberculosis* by cultivation from the gastric content, such diagnosis might have been permitted to stand.

"Tuberculous Rheumatism" an Expression of Hypersensitivity.

It is scarcely conceivable that the arthritic and myalgic symptoms which, occurring singly or together in occasional cases of primary tuberculous infection, have led to the recognition of the clinical entity "tuberculous rheumatism" are due to the immediate activity of tubercle bacilli within the joints or periarticular tissues. Such a situation could not be sustained wtihout an extraordinary degree of attenuation of the bacilli, or an exceptional relationship between the tissues of the host and the intruding micro-organisms, far removed from that which prevails in the destructive course of tuberculous arthritis. Rather is the phenomenon of tuberculous rheumatism to be regarded as a manifestation of the hypersensitive state, to which indeed Arnold Rich (1946) would refer all the specific constitutional symptoms of tuberculosis. Rich insists that the tubercle bacillus does not, *in vitro*, elaborate any substance that is appreciably toxic for the normal body, and that the injection of large amounts of tuberculo-protein is tolerated with no symptomatic response by both experimental animals and human beings not sensitized to the tubercle bacillus or its products. Tissue damage and constitutional symptoms supervene on the establishment of the hypersensitive state, a sequence which, though preeminent and most impressive in tuberculosis, is doubtless operative in other infections also.

Erythema nodosum, when it occurs in the course of primary tuberculous infection, is an outward and visible sign of the hypersensitive state, and the tuberculous rheumatism syndrome another; the two expressions of hypersensitivity may occur singly, as in one, or together as in the other of the two children the clinical and laboratory findings concerning whom provide the basis for this discussion. Considered in relation to the number of persons in whom a focus of tuberculous disease, recognized or occult,

is established, neither *erythema nodosum* nor tuberculous rheumatism is a frequent occurrence, and the factors which determine the low incidence, and whether either or both of the two stigmata will appear, remain matters for speculation. It may be recalled that pains in the joints are a feature of serum sickness, and arthralgia figures in the symptom complex of the systemic reaction induced by the injudicious injection of tuberculin in the presence of hypersensitivity to the tubercle bacillus and the products of its disintegration.

As the result of many indefatigable researches, conspicuous among which are those of Coburn (1936), the role of the group A hæmolytic streptococcus as the ultimate ætiological agent in acute rheumatism is scarcely to be questioned, but the mechanism underlying the characteristic clinical course and morbid changes of rheumatic fever is not yet clearly defined. As is well known, an interval commonly elapses between the occurrence of acute streptococcal tonsillitis and the onset of rheumatic fever, and although the hypersensitive state and the time required for its induction may be invoked to explain the curious delay in the rheumatic development, the question why a proportion only of persons infected with hæmolytic streptococci should react in this peculiar manner remains unanswered.

Coburn has shown that in those individuals in whom acute rheumatism supervenes on streptococcal infection of the throat there is a very slow rise in the titre of antistreptolysin and other immune bodies, as compared with that demonstrable in the sera of those who dispose of their streptococcal infections summarily and without rheumatic sequelæ. The slow serological reaction to the initial streptococcal infection observed in subjects of rheumatic fever represents an inadequate response on the part of the normal defence mechanism, and permits the establishment of streptococcal foci in the tissues. The protracted liberation of antigen, derived from the disintegration of the microorganisms in such foci, renders the cells of the bodily tissues hypersensitive by an accumulation of cell-bound antibody, which eventually reacts with the provocative antigen, violently or more moderately, according to the degree of hypersensitivity and the amount of antigen liberated on any occasion, and thus determines the rheumatic *dénouement*.

Whether the allergic hypotheses advocated by many as explanatory of the sequence of events in acute rheumatism be accepted or not, it is clear from the work of Coburn and his associates that there is some aberration in the immunological reactions of those persons in whom rheumatic phenomena supervene on infection of the throat by group A hæmolytic streptococci. That a similar vagary in the immune response to tuberculous infection may occasionally influence the clinical course of tuberculosis seems not altogether improbable. It has been shown by A. B. Baker (1935) that there is no parallelism between the titre of immune antibodies specific for the tubercle bacillus, as gauged by the complement-fixing antibody, and the degree of tuberculin sensitivity, and a lag in the immunity mechanism, with consequent delay in bringing the output of antigen under restraint, may result in a situation scarcely to be distinguished from that which has been formulated by the exponents of the allergic hypothesis of the ætiology of rheumatic fever.

Even if the considerations advanced should embody a correct conception of the pathogenesis of rheumatic manifestations as they follow streptococcal infection usually, and tuberculous infection occasionally, it still remains a problem why the essentially systemic hypersensitive reaction on which it is based should wreak its most obvious effects on the synovia of joints, the endocardium and pericardium, and cardiac and skeletal muscle. In this connexion Hadfield and Garrod (1947) note the work of certain German investigators who designed experiments to show that the vulnerability of the structures named is to be referred to the "physiological trauma" to which they are subjected by the necessity for constant movement.

References.

Baker, A. B. (1935), "Complement Fixation as Related to Resistance and Allergy in Experimental Tuberculosis", *The American Review of Tuberculosis*, Volume XXXI, page 55.

Coburn, A. F. (1936), "Observations on the Mechanism of Rheumatic Fever", *The Lancet*, Volume II, page 1025.

Findlay, L. (1920), "'Rheumatisme Tuberculeux' or Tubercular Rheumatism", *Glasgow Medical Journal*, Volume I, page 241.

Hadfield, G., and Garrod, L. P. (1947), "Recent Advances in Pathology", Fifth Edition, page 130.

Poncet A., and Le Riche, R. (1909), "*Le rheumatisme tuberculeux*", Paris.

Rich, A. R. (1946), "The Pathogenesis of Tuberculosis", Charles C. Thomas, Springfield, Illinois, pages 6 and 382.

Sheldon, W. (1946), "Tuberculous Rheumatism", *The Lancet*, Volume I, page 119.

Erythema Nodosum.

Erythema nodosum was a feature of the illness of eight of the series of 162 children for whom the diagnosis of tuberculosis was established by the cultivation of tubercle bacilli from the gastric content. All reacted to tuberculin. Radiographic observations synchronous with the eruption are lacking for one child in the group (number 135) by reason of the fact that the appearance of the painful cutaneous nodes antedated the boy's first attendance at the Children's Hospital by a period of three months. In the investigation of the other seven thoracic radiographs were requested and provided in the florid phase of the eruption.

The radiograph of the little girl represented by the number 68 was interpreted as indicative of a pneumonic process, of doubtful ætiology, affecting the apical portion of the right lung. The report made no mention of abnormal shadows referable to the hilar lymph nodes. In a radiograph taken fifteen days later the apical shadow was seen to have dispersed to a large extent, and the child was discharged after two months in hospital, relatively well, *Mycobacterium tuberculosis* having been recovered from her gastric content in the interval.

The radiograph of another little girl (number 76), the third member of the group, revealed an irregular patch of bronchopneumonic consolidation, situated medially in the lower lobe of the right lung. Again the report was non-committal regarding the probable ætiological factor, and again the hilar lymph nodes excited no comment. The radiological reports concerning all of the remaining five children recorded the presence of hilar lymph node enlargement in definite terms, and with equal decision stated that there was no detectable disease focus in the pulmonary parenchyma.

The association of hilar lymph node enlargement with *erythema nodosum* has recently been the subject of an investigation to which C. Clifford Johnson, Norbert O. Hanson and C. Allen Good (1951) were stimulated by the observation that within a period of four months three patients at the Mayo Clinic exhibited demonstrable enlargement of the pulmonary hilar lymph nodes synchronously with the eruption of *erythema nodosum* and lost all signs of both cutaneous and pulmonary pathological change while they were still under surveillance.

In order to pursue the possibility that pulmonary hilar lymph node enlargement might be linked with *erythema nodosum* as a manifestation of that state, taking its place with the cutaneous nodes, painful joints, fever and malaise which constitute the syndrome, the authors named searched the records of the Mayo Clinic until they assembled details of 100 cases of *erythema nodosum*, in which the dermatological diagnosis could not be questioned, and in which radiographic investigation had been carried out. It is interesting to note that of the 100 patients 30 showed no sign of other disease associated with the *erythema nodosum*, 20 had an unspecified infection of the upper respiratory tract, and—a surprising finding—frank tuberculosis could be implicated in only two. A variety of associated conditions, chiefly infective, was recorded for the remainder, and it is noteworthy that 15 of the patients were sensitive to drugs, which were regarded as causal agents.

Enlargement of the hilar lymph nodes, bilateral in all except one instance, was demonstrated radiographically in nine patients of the series, and in five concerning whom it was possible to make later observations, the hilar shadows

dispersed within a period of a few months. In none of the nine could any disease process other than *erythema nodosum* be found to which the enlargement of the hilar lymph nodes might be attributed. The suggestion was therefore advanced that enlargement of the pulmonary hilar lymph nodes might be one expression of *erythema nodosum* itself, a condition of notoriously non-specific ætiology.

The findings of Johnson, Hanson and Good relate chiefly to adults, and whatever of truth may eventually be found to be embodied in what they describe as their tentative belief, when it occurs in a child who reacts to tuberculin *erythema nodosum* must be regarded as a manifestation of tuberculosis until it is proved otherwise. No one familiar with the work of Wallgren and others of the Scandinavian school will dispute this statement, but it must be allowed that ætiological factors vary in different parts of the world. In certain regions of California and Arizona, in the United States of America, coccidiomycosis is conspicuously in the forefront of ætiological factors in *erythema nodosum*. Kerley (1942, 1943) has drawn attention to the fact that a nodular eruption, very similar to if not identical with *erythema nodosum*, sometimes figures in the clinical history of sarcoidosis. The waning influence of rheumatic infection on opinion relating to agents provocative of *erythema nodosum* is to be attributed in large measure to findings such as those of Perry (1944), who in a review of 112 subjects of *erythema nodosum*, found 10 only who had suffered an attack of acute rheumatism; only two of these persons sustained a second attack, and in five others there was evidence of tuberculosis. Since these 10 cases provided the only examples observed by Perry among over 1000 cases of acute rheumatism, the validity of many previous observations connecting the two entities would seem to be seriously challenged.

The view that *erythema nodosum*, when referable to tuberculosis, is a manifestation of hypersensitivity to the tubercle bacillus and/or its disintegration products gains support from the fact that in those comparatively few instances in which it has been possible to determine the date and circumstances under which primary tuberculous infection was acquired, the nodular eruption has appeared after an interval which corresponds with that required for the development of the hypersensitive state, namely, thirty to sixty days. Observations in this regard by W. Mascher, of Sweden (1943), render it difficult to escape the conclusion that *erythema nodosum* is at least very often the consequence of exposure to tuberculous infection within the preceding two months. Elsewhere (1950) I have advanced argument in support of a suggestion that the immunological processes underlying the tuberculin reaction and *erythema nodosum*, both manifestations of hypersensitivity, are not identical, the former being the very prototype of the reaction expressive of the hypersensitivity induced by bacterial infection, and *erythema nodosum* having anaphylaxis as its basis.

References.

Johnson, C. C., Hanson, N. O., and Good, C. A. (1951), "Erythema Nodosum: The Possible Significance of Associated Pulmonary Hilar Adenopathy", *Annals of Internal Medicine*, Volume XXXIV, page 983.

Kerley, P. (1942), "Significance of Radiological Manifestations of Erythema Nodosum", *British Journal of Radiology*, Volume XV, page 155.

——— (1943), "Ætiology of Erythema Nodosum", *British Journal of Radiology*, Volume XVI, page 199.

Mascher, W. (1943), *"Das Erythema Nodosum beim Erwachsenen als Symptom der Tuberkulosen Primärinfektion und seine Folgezustände"* (review), *British Medical Journal*, Volume II, 1944, page 857.

Perry, C. (1944), "The Ætiology of Erythema Nodosum", *British Medical Journal*, Volume II, page 843.

Webster, R. (1950), "Phases of Tuberculosis in Childhood", "Studies in Pathology", presented to Peter MacCallum, Melbourne University Press, page 145.

Phlyctenular Conjunctivitis.

Tuberculosis as the basis of phlyctenular conjunctivitis was demonstrated in five children by the cultivation of *Mycobacterium tuberculosis* from the gastric content. In one (number 17) the phlyctenular ophthalmia arose several months after clinical, radiological, and bacteriological evidence had abundantly proved the tuberculous nature of the arthritis affecting the hip joint which initially brought the boy under observation. Phlyctenular kerato-conjunctivitis was also an incident in the illness of an infant aged fifteen months, the ophthalmia appearing three and a half months after the baby's admission to hospital, at a time when radio-opacity of almost the whole of the upper lobe of the left lung was demonstrable, and after the nature of such opacity had been proved by the recovery of tubercle bacilli from the gastric content. In the remaining children to exhibit phlyctenular ophthalmia, good general health, household contact with tuberculosis, and tuberculin sensitivity were features common to all three.

A sore right eye, of two weeks' duration, was the immediate cause of the presentation at the out-patients' department on June 6, 1942, of number 24, a small girl, aged two years and nine months. At the time her mother was supporting a pneumothorax induced as collapse therapy for pulmonary tuberculosis. A report on the thoracic radiograph of the child, dated October 8, 1942, noted "a few calcified glands in the hilum", and stated specifically that there was no evidence of active infiltration of the parenchyma of the lung. Further X-ray examinations, respectively one month and six months later, failed to reveal any disease process in the pulmonary parenchyma, but specimens of gastric content taken on dates synchronizing with the first of these radiographs and within a few days of the second, yielded cultures of *Mycobacterium tuberculosis* in both instances.

K.B. (number 123), aged three years, developed phlyctenular ophthalmia while under observation for enlargement of the cervical lymph nodes of several months' duration. The presumption of tuberculosis was never confirmed with respect to the cervical lymph nodes, *Staphylococcus aureus* appearing in cultures of purulent material eventually evacuated from them. From the gastric content, however, *Mycobacterium tuberculosis* was cultivated, despite radiological opinion that the lungs were free from pathological change.

T.W. (number 148), aged six years, whose mother had recently been discharged from a sanatorium, presented with phlyctenular kerato-conjunctivitis on January 26, 1950. A thoracic radiograph of the same date revealed an opacity of triangular shape situated posteriorly in the lower lobe of the left lung; the shadow was regarded by the radiologist as suggestive of pneumonitis, or possibly segmental collapse. It was considered that the radiograph provided no specific evidence of tuberculosis, but *Mycobacterium tuberculosis* was cultivated from a specimen of gastric content withdrawn seven days later (February 2, 1950). A radiograph of March 20 showed the shadow observed in the initial film of January 26 to have dispersed, and thereafter five successive radiographs, extending over a period of twelve months, failed to show evidence of any pathological process affecting either the parenchyma of the lungs or the hilar lymph nodes. In the meantime *Mycobacterium tuberculosis* was recovered from a second specimen of gastric content submitted for examination on November 20, 1950. The lack of radiographic signs of tuberculosis in the presence of cultural findings of a positive nature in this respect caused this little boy to be the subject of much comment, but the matter is not of present concern.

Although an impressive volume of indisputable evidence has now been accumulated to establish the significance of tuberculous infection as the outstanding ætiological factor in phlyctenular kerato-conjunctivitis, this condition is not to be confused with that inflammatory affection of the conjunctiva which exhibits the characteristic histology of tuberculous granulation tissue, is associated with enlargement and caseation of the corresponding preauricular lymph node, and is properly described as tuberculous conjunctivitis. I can recollect only two examples of tuberculous conjunctivitis in this sense, both derived from the ophthalmic clinic of the late Dr. Mark Gardner. The epithelioid cell reaction, giant cells, and caseation clearly to be read in the microscopic sections of biopsy snippings of granulation tissue, combined with an enlarged and caseous preauricular lymph node in each instance to stamp the pathological process as an ocular primary complex. By contrast with such distinctive histology, there is nothing specific in the microscopic structure of the phlycten, this nodular reaction in the conjunctiva showing nothing more helpful microscopically than a nondescript collection of small round cells. Whereas tuberculous conjunctivitis is due to the activity of tubercle bacilli demonstrable in the

lesions, phlyctenulosis is to be regarded, like *erythema nodosum*, as a manifestation of the hypersensitive state, the source of the sensitization being most frequently, but not necessarily, tuberculous infection.

Phlyctenular Conjunctivitis and the Hypersensitive State.

The conception of phlyctenular kerato-conjunctivitis as a reaction of hypersensitivity dates from the application of Calmette's ophthalmo-tuberculin test, and ensuing observations of severe conjunctivitis and keratitis, similar to the clinical entity phlyctenular ophthalmia, frequently precipitated by the instillation of tuberculin into the conjunctival sac. Even earlier, and quite apart from the local effect of tuberculin on the eye, it had been noted that ocular phlyctenules were prone to erupt in the course of treatment by subcutaneous injections of tuberculin in the drastic dosage which distinguished this form of therapy in its early days. Of a piece with such observations was that of Bickerton (1936), who recorded the appearance of phlyctenules after the operative removal of tuberculous cervical lymph nodes.

The occurrence of phlyctenulosis as an episode in diagnostic and therapeutic measures involving the use of tuberculin stimulated much experimental work designed to verify the inference that phlyctenular ophthalmia was essentially a reaction of hypersensitivity. It has been found possible to excite a phlyctenular reaction by means of the appropriate antigen in animals sensitized to a specific chemical, such as peptone or casein, or to a specific micro-organism such as the tubercle bacillus or the staphylococcus. The maximum and most consistent effect is obtained by the use of the specific allergen as the provocative agent, but it would appear that specificity of the allergen is not a rigid and inflexible condition. Rosenhauch (1910), for instance, induced ocular phlyctenules of the histological structure of those which occur in human beings by instilling living or dead staphylococci into the conjunctival sacs of rabbits sensitized by infection with the bovine type of tubercle bacillus, although the effect of the staphylococcal antigen was not as consistent and certain as that attending the use of tuberculin as the excitant. The conclusion to be drawn from an exhaustive review of experimental studies by Arnold Sorsby in his Hunterian Lecture (1942) is that the phlyctenular reaction derives from an exciting factor operating in a sensitized medium. Sensitization may be induced experimentally by a variety of agents, of which tuberculous infection is one. The most effective, though not essential exciting factor, is the sensitizing agent.

An imposing array of incontestable evidence that tuberculous infection is preeminent among the ætiological factors contributing to phlyctenulosis is to be found in the relevant literature. Data such as the high incidence of tuberculin sensitivity—approximately 80%—in children affected with phlyctenular kerato-conjunctivitis, the only little less frequency (72%) with which radiographic signs of tuberculous chest lesions have been demonstrated, the family history of tuberculosis commonly ascertainable, and the unfavourable developments of a tuberculous nature in "phlycten" patients, combine with the clinical resemblance of phlyctenular ophthalmia to the unhappy sequelæ of the Calmette ophthalmo-reaction of an earlier day and a notable incidence of previous phlyctenulosis in adults suffering from tuberculosis, in an impressive aggregate of evidence which is scarcely to be gainsaid. The importance of tuberculous infection as a factor in phlyctenular ophthalmia is underlined by laboratory results such as the cultivation of tubercle bacilli from the gastric content of the five children considered in this report.

Strictly speaking, phlyctenules are not tuberculous lesions, though intimately related to tuberculous infection in the majority of instances, and no doubt the unsatisfactory term "paratuberculous" was intended to convey some such meaning. Although tuberculous infection is by common consent predominant among sensitizing agents, the nodular reaction in the conjunctiva which is the phlycten has no distinctive histology, and has been observed in conjunctivitis of such ætiologically distinct types as those of the Koch-Weeks bacillus and the diplobacillus of Morax-Axenfeld. But although the preeminence of tuberculous infection as the underlying factor is incontrovertible, experimental findings seem to suggest that specificity in the provocative antigen is not essential. There would seem to be little doubt, however, that in children who have incurred tuberculous infection by household contact, phlyctenular ophthalmia is a reaction induced by the impact on the eye of sputum spray or dust derived from the environment.

That tuberculin sensitization, though most frequently the basis of phlyctenulosis, is not a *conditio sine qua non* has been shown by results attending the use of diverse antigens, and Sorsby (1942) has defined, from clinical observation at White Oak Hospital, a group of cases of phlyctenular ophthalmia, embracing 10% to 15% of the total, in which there is no evidence of tuberculous infection. Experience at the institution named has shown that non-tuberculous phlyctenular ophthalmia tends to follow a distinctive clinical course, the disease being protracted, relatively resistant to treatment, and exhibiting a decided tendency to a serious degree of scarring of the cornea. Thus clinical evidence is in accord with experimental as regards the non-specificity of the phlycten reaction. In this respect phlyctenulosis resembles *erythema nodosum*, as it does in its greater incidence in the female sex.

References.

Bickerton (1936), cited by Arnold Sorsby, Hunterian Lecture.

Rosenhauch (1910), cited by Arnold Sorsby, Hunterian Lecture.

Sorsby, A. (1942), "The Ætiology of Phlyctenular Ophthalmia", Hunterian Lecture, Royal College of Surgeons, *British Journal of Ophthalmology*, Volume XXVI, pages 159 and 189.

MILIARY AND MENINGEAL TUBERCULOSIS.

Mycobacterium tuberculosis was cultivated from the content of the fasting stomach of 26 children in whom the clinical diagnosis of tubercuous meningitis was confirmed by cytological and biochemical findings in the cerebro-spinal fluid, and the cultivation of *Mycobacterium tuberculosis* from the fluid withdrawn by lumbar puncture in every instance. The majority date back to pre-streptomycin days, but of six children in the group who received the benefit of streptomycin therapy, two recovered. Autopsy was not permissible in three instances. Of the 21 children who died from tuberculous meningitis and were examined *post mortem*, 15 exhibited a severe degree of miliary tuberculosis, and six meningeal tuberculosis unaccompanied by any macroscopically recognizable miliary sowing in the thoracic or abdominal viscera. That two of these half-dozen children had passed through a phase of miliary sowing resolved by streptomycin therapy is clear from the unequivocal character of the evidence provided by their thoracic radiographs. The number of children yielding *Mycobacterium tuberculosis* from the gastric content and dying of meningeal tuberculosis with no associated miliary tuberculosis is therefore to be reduced to four.

A review of any adequate series of autopsies will show, as I can certify from experience of many years, (i) that there may be no meningitis in the presence of miliary tuberculosis of even maximum intensity, and (ii) that meningitis may occur in the total absence of miliary tuberculosis. The relatively small group of 30 children under discussion as having provided cultures of *Mycobacterium tuberculosis* from the gastric content furnishes examples which affirm the truth of both of the foregoing statements, for against the four patients who exhibited meningeal tuberculosis independently of miliary tuberculosis are to be considered four others in whom the reverse situation obtained, that is, an extreme degree of miliary tuberculosis with no associated tuberculous meningitis. The intensity of the miliary sowing is emphasized in the post-mortem records of each of these four children, yet there was no meningitis.

Pathogenesis of Meningeal Tuberculosis.

It was the consideration of such occurrences that led Rich and McCordock (1933) to challenge, with a large measure of

success, the apparently impregnably established doctrine that tuberculous meningitis was but a phase of miliary tuberculosis, and referable to direct hæmatogenous infection of the leptomeninges in the course of the bacillæmia inseparable from this catastrophe. Such belief was based on the undoubtedly frequent coincidence of tuberculous meningitis and miliary tuberculosis, especially in infants and very young children. The alternative and forcefully maintained thesis of Rich and McCordock was that tuberculous meningitis arose independently of miliary tuberculosis and was to be attributed to infection of the meninges by the discharge of the contents of a contiguous caseous focus into the subarachnoid space. This view gained general, though not unqualified, support from an investigation of the question by MacGregor and Green (1937). Another worker who endeavoured to solve the problem in pathogenesis which had arisen concerning a process formerly regarded as clearly understood was McMurray (1944), who reported his findings in a meticulous study of the brains of eleven children, the immediate cause of whose death was tuberculous meningitis. Of the eleven brains examined, meningeal or juxtameningeal foci were found in ten; two of such parent foci were situated in the brain substance and eight in the leptomeninges, either in a sulcus or in the vicinity of a main cerebral artery. In ten of the eleven cases, therefore, the immediate forerunner of tuberculous meningitis was a precipitating focus inside the skull. Five only of the eleven subjects of meningeal tuberculosis selected for investigation by McMurray exhibited coexistent miliary tuberculosis in the viscera generally, and in the brains of four were found caseous foci, of an age appearance which indicated that they were of longer standing than the meningeal tubercles. In none of the five did the appearances of the meningeal and visceral miliary lesions correspond with respect to age, from which observation the inference was that the two processes, meningeal tuberculosis and disseminated miliary tuberculosis, had arisen independently. In two cases indeed, the meningitis appeared to have been initiated prior to the miliary spread.

It was demonstrated by Rich and McCordock (1933) that the intravascular injection of massive doses of virulent tubercle bacilli in experimental animals regularly caused widely distributed miliary tuberculosis, but did not induce a simultaneous exudative meningitis. The immediate result, as it affected the meninges, of experimental infection by way of the blood stream, was the production of sparsely distributed discrete tubercles, as opposed to acute exudative meningitis—a regular and consistent finding, which was in line with the experimental determination by Brickner (1927) that the pia-arachnoid was to be grouped with the pleura, peritoneum and pericardium, the heart, pancreas and thyroid, as tissues and organs which held and stored relatively small fractions of circulating particulate matter. The distribution of tubercles in miliary tuberculosis and that of inert particulate matter introduced into the blood stream exhibit a degree of parallelism which may be appreciaed from the fact that tissues such as the pleura, pericardium, and peritoneum, which have been shown to arrest comparatively few circulating particles of colloidal carbon, are seldom involved to any extent in miliary tuberculosis. The museum of pathology at the Children's Hospital, Melbourne, has only one specimen of tuberculous pericarditis, deriving not from miliary tuberculosis, but from the discharge into the pericardial sac of the infective content of an adherent caseating mediastinal lymph node (Figure I). Rich and McCordock further showed that the exudative inflammatory reaction of tuberculous meningitis, when it did follow intravascular injection of tubercle bacilli, did not supervene until after the lapse of the several weeks required for the caseation, softening, and discharge of the content of one or more of the induced juxtameningeal foci into the subarachnoid space of an animal rendered hypersensitive in the interval. As opposed to the result of intravascular injection, when tubercle bacilli were introduced directly into the subarachnoid space of a sensitized animal by way of the optic foramen, the diffuse inflammatory reaction characteristic of tuberculous meningitis followed immediately.

If tuberculous meningitis is not to be regarded as a concomitant of miliary tuberculosis, how is the undoubted frequency of the coincidence of miliary tuberculosis and tuberculous meningitis in children, and in infants especially, to be explained? Infants and very young children have little opportunity to supplement their genetic endowment of resistance with any degree of acquired immunity to tuberculous infection, and in autopsies in which miliary tuberculosis and tuberculous meningitis are found to coexist, it is generally observed that the primary lesion, or the lymph node component of the primary complex, is progressive and extensive. It is not unreasonable to suppose, therefore, that under such conditions there is a greater probability of the development in the brain and meninges of caseous foci prone to undergo rapid softening and to discharge bacilli into the subarachnoid space.

Experience at the Children's Hospital, Melbourne.

In the course of my years of experience in the pathology department of the Children's Hospital I have performed many autopsies which disclosed a state of miliary tuberculosis with attendant tuberculous meningitis, but I learned to regard this association as not inevitable, and not to be surprised by the occasional autopsy in which miliary tuberculosis was unaccompanied by tuberculous meningitis, or conversely, tuberculous meningitis occurred independently of disseminated tuberculosis. In autopsies illustrative of each of these situations I have often located, in a cerebral sulcus or in the leptomeninges, a softened caseous focus, which, if it had not actually ruptured, seemed from its character and situation to be charged with menace as a threshold of entry of tubercle bacilli to the subarachnoid space. There have been many occasions also on which I have been unable to identify a nidus of tuberculous infection in cortex, meninges, or cranial bones as the immediate provocative lesion in tuberculous meningitis. Failure to find a precipitating focus at autopsy, however, is in no sense conclusive regarding its absence, and many brains have I put aside against a time when I should be enabled to institute the minute search often essential to the discovery of an intracranial parent focus in tuberculous meningitis. So many intentions in this regard were frustrated by the unremitting pressure of pathology of the living that I am unable, from my own records, to compile a documented statement as to the proportion of cases of tuberculous meningitis in which a precipitating intracranial focus was present.

Evidence for the statement that the overwhelming bacteriæmia underlying extreme degrees of miliary tuberculosis does not imply diffuse meningeal tuberculosis as a necessity is provided in the present series by four children to whom reference has already been made. Two were infants aged ten and fourteen weeks respectively, the third was twenty-three months of age, and the fourth twenty-nine months. All four eliminated acid-fast bacilli, proved by subsequent cultivation to be *Mycobacterium tuberculosis*, in numbers sufficient to render them readily detectable by the microscopic examination of smear preparations of the gastric content. It is not possible to overstate the density of the sowing of miliary tubercles in the lungs, liver, and spleen of each of these four children, yet in none was there any trace of the plastic basal exudate and excess of cerebro-spinal fluid of tuberculous meningitis in the generally accepted sense of the term. From the detailed autopsy records of these children, however, the interesting fact emerges that in three of the four the stage was set for a culminating meningitis by the establishment of intracranial metastatic foci, the discharge of the contents of which would have given tubercle bacilli the access to the subarachnoid space which they had apparently been unable to effect by vascular penetration.

The autopsy of number 29, for instance, M.B., an infant, aged ten weeks, one of whose clinical features was an aural discharge in which acid-fast bacilli were detected prior to death, revealed bilateral tuberculous mastoiditis.

Number 46, B.T., aged twenty-three months, an aboriginal child, in whom native resistance might have been expected to be minimal or non-existent, exhibited miliary tuberculosis of a degree of severity which may be gauged from Figure II;

there was no exudative meningitis, but a caseating point was discovered on the surface of the brain near the right occipital pole. A smear preparation of the material obtained on a knife-point from this caseous lesion, the rupture of which appeared imminent, showed numerous tubercle bacilli; two similar caseous foci were discovered elsewhere on the surface of the brain.

In the case of number 50, N.M., aged fourteen weeks, there was found at autopsy, after some search, a small caseous point in the cortex in the parieto-occipital region of the left cerebral hemisphere. The nodule was not more than 3·0 millimetres in diameter, and its contents, smeared from a knife-point, were found to include very many tubercle bacilli. Again there was no exudative meningeal tuberculosis. A further interesting observation with respect to this infant was the presence of two small caseating foci, of slightly larger than miliary dimensions and apparently poised for rupture, in the serous pericardium on the anterior aspects of the right and left ventricles respectively. Rupture of one or other of these focal lesions having been averted, there was no diffuse pericarditis.

FIGURE I.
Tuberculous pericarditis. Caseating mediastinal lymph nodes: that indicated by arrow has discharged its softened contents into the pericardial sac.

The view, for long apparently incontestable, that tuberculous meningitis resulted from the lodgement in the meninges of tubercle bacilli which had forced the passage of the choroid plexus and meningeal vessels during the bacillæmia of miliary tuberculosis, rested not only on the frequent coincidence of the two processes, but on authoritative and abundantly substantiated studies which demonstrated the constancy and extent of destructive tuberculous lesions affecting the meningeal vessels, particularly arterioles.

Vascular Lesions in Meningeal Tuberculosis.

An early and exhaustive investigation of the vascular changes in tuberculous meningitis was that of Hektoen (1886), and from the review of antecedent relevant literature in the report of that author it is to be noted that histological studies on the part of Huguenin, and of Cornil, had determined tuberculous arteritis and phlebitis in the lesions of tuberculous meningitis before Koch's announcement of his discovery of the tubercle bacillus. Hektoen presented his work as having demonstrated that the morbid changes in tuberculous meningitis include tuberculous endarteritis, characterized by the formation of intimal tubercles and a diffuse subendothelial intimal cellular infiltration and proliferation. He regarded the

intimal lesions as indicative of implantation of tubercle bacilli from the blood stream, and described the intimal infiltration as frequently advancing through the muscular wall and adventitia of the vessel to effect caseating necrosis of the whole of the vascular wall in the particular segment affected. Hektoen noted, conversely, that identical lesions, no less destructive in their effects, might be initiated in the adventitia of arterioles and progress through the media to the intima from without inwards. He found the veins to be involved in a similar inflammatory-necrotizing process, and attributed the tuberculous phlebitis to extension of infection from adjacent extravascular or arterial foci.

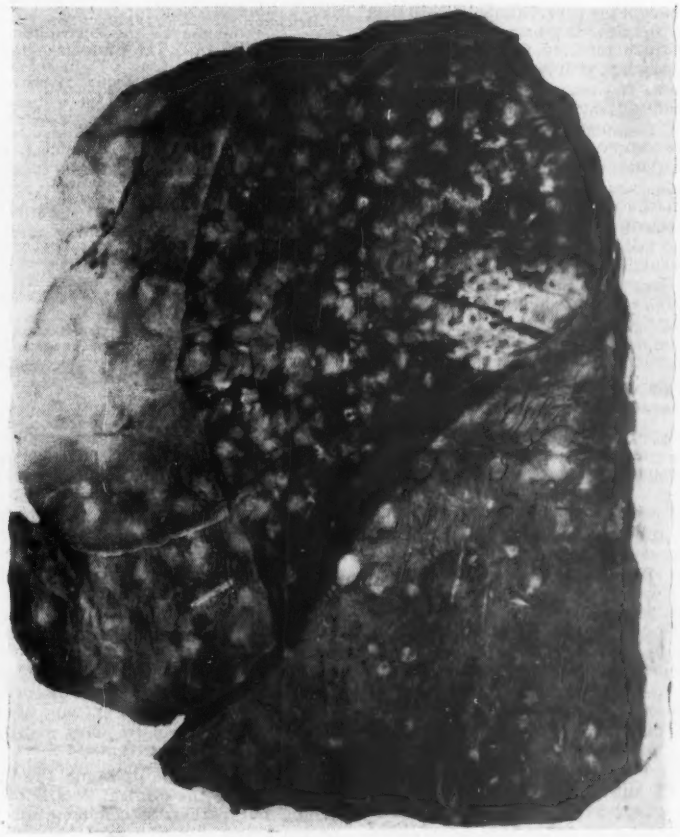

FIGURE II.

Acute caseating miliary tuberculosis: infant, aged twenty-three months: comparable lesions in other viscera, but no exudative tuberculous meningitis. By courtesy of the Melbourne University Press.

In the sixty-six years which have elapsed since the publication of Hektoen's work many explorations of the same field by different workers have in no way impugned the truth of his findings nor shaken their validity; they undoubtedly convey a strong suggestion that meningeal tuberculosis is induced directly by blood-borne tubercle bacilli. In propounding their thesis relating to its pathogenesis, Rich and McCordock recognized the crucial importance of the vascular lesions of tuberculous meningitis, and directed particular attention to the manner in which the meningeal vessels became involved.

In the examination of pathological material derived from human subjects of tuberculous meningitis which was unaccompanied by miliary tuberculosis, and definitely the result of extension of infection from a local focus, it was found that the vascular changes were present just as abundantly and characteristically as they occur when tuberculous meningitis is associated with the blood stream infection inherent in miliary tuberculosis.

Experimental studies in which the meninges of rabbits were infected with tubercle bacilli directly by way of the optic foramen provided evidence in support of the contention that the character of the lesions in the blood vessels in tuberculous meningitis could not be regarded as proof that the responsible bacilli reached the meninges by way of the blood stream. In such animals, with meninges infected directly and hæmatogenous infection precluded, there ensued exudative meningitis exhibiting all the characteristic features of tuberculous meningitis as it occurs in the human subject.

In discussing the vascular lesions as they observed them in directly induced experimental tuberculous meningitis, Rich and McCordock emphasized that, as in human tuberculous meningitis, the bacilli showed a pronounced tendency to congregate about the small meningeal blood vessels, and that cells accumulated in and about the walls of such vessels in a manner identical with that which was commonly observed in tuberculous meningitis affecting the human being. Microscopic studies of the meninges of animals killed at varying intervals after infection showed that the lesions began at the periphery of a vessel and extended from without inwards; once well developed, however, the vascular changes were indistinguishable from those of human tuberculous meningitis.

The occurrence in their experimental animals, in which tuberculous meningitis was induced by direct implantation of tubercle bacilli on the surface of the brain, of ependymal roughening similar to that to be observed regularly in human cases of tuberculous meningitis—another feature which has been called into evidence in support of the direct hæmatogenous origin of meningeal tuberculosis—led Rich and McCordock into closely reasoned argument by which they maintained that tubercle bacilli liberated into the cerebro-spinal fluid from the surface of the brain gradually find their way by retrograde conveyance to the ventricles, where they may initiate ependymal tubercles and tuberculous lesions of the choroid plexus.

In the last analysis of course tuberculous meningitis must be of hæmatogenous origin; the point at issue has been whether the meninges are infected directly from the blood stream in the course of miliary tuberculosis or indirectly by the discharge of the contents of a contiguous metastatic focus established during an episode of bacillæmia, such as is known frequently to attend primary infection, and to occur at intervals during the progress of clinically active tuberculous disease. It would seem that there can be no doubt that tuberculous meningitis very commonly arises from the eruption of a precipitating focus, and as regards the possibility of its being the direct result of the bacillæmia of miliary tuberculosis, one feels that if tubercle bacilli present in force sufficient to produce such extreme grades of miliary tuberculosis as were exhibited by the children represented by the numbers 15, 29, 46, and 50 could not "gate-crash" the cerebro-spinal space from the blood stream, they probably never do so.

Meningeal Tuberculosis as Precursor of Miliary Tuberculosis.

It has been proposed that tuberculous meningitis might precede and give rise to miliary tuberculosis, an idea which on examination seems not so improbable as its first impact might suggest. Until the advent of streptomycin therapy determined some negative cultural findings, it was my experience that tubercle bacilli were susceptible of cultivation from the cerebro-spinal fluid of every child affected with tuberculous meningitis; the inference is that tubercle bacilli are always free in the cerebro-spinal fluid, and in the normal course of its circulation this vehicle may be expected to convey the microorganisms to the venous system. Hektoen (1886) in his classic study laid emphasis on the changes he observed in the veins of the pia in tuberculous meningitis, stating that in all instances the veins, large and small, showed diffuse or circumscribed infiltrations of the walls; such infiltrations invariably proceeded from changes in the neighbourhood, as in an adjacent artery. He described caseation, giant cells, and disintegration of the infiltrated venous walls, demonstrated the presence of tubercle bacilli in the lesions, and expressed himself as having no doubt that generalized miliary tuberculosis might develop secondarily to tuberculous meningitis as the result of dissemination of tubercle bacilli from the extensive and constant lesions in the pial veins.

An instance of miliary tuberculosis referable to implication of the pial veins in eroding tuberculous foci was observed in a child aged two years, whose brain has been preserved in the museum of pathology of the Children's Hospital and photographed to provide Figure III. The child was presented at a meeting of the Melbourne Pædiatric Society by the late Dr. J. W. Grieve (1943). The most conspicuous feature of the autopsy was subarachnoid hæmorrhage. A number of small caseous foci, somewhat larger than the miliary tubercles of tuberculous meningitis, were dotted about the convexity of the cerebral hemispheres of both sides, and it was particularly to be noted that there was none of the basal exudate and excess cerebro-spinal fluid of tuberculous meningitis. It appeared most probable that instead of discharging their content into the subarachnoid space to precipitate tuberculous meningitis, one or more of the "parent foci" elected to erode a pial vein and thereby liberate tubercle bacilli into the blood stream. The clinical sequence of events was in accord with this view, for at the outset of an illness initiated by drowsiness, muscular twitchings and hemiparesis there was no conclusive indication of miliary tuberculosis in a thoracic radiograph; another taken six days later provided evidence on this point which could scarcely be doubted, and the presence of miliary tuberculosis was eventually substantiated at autopsy.

The morbid anatomy of tuberculous meningitis, as it now appears modified by streptomycin therapy, has been clearly and concisely described by Alan L. Williams (1951). Included in his report are photomicrographs chosen to illustrate the occlusive nature of the vascular changes, from which follows the necessity for early recognition of tuberculous meningitis, and prompt institution of streptomycin therapy if irreparable loss of brain tissue is to be avoided.

References.

Brickner, R. M. (1927), "The Role of the Capillaries and their Endothelium in the Distribution of Colloidal Carbon by the Blood Stream", *The Bulletin of the Johns Hopkins Hospital*, Volume XL, page 90.

Grieve, J. W. (1943), THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, pages 451 and 544.

Hektoen, L. (1886), "The Vascular Changes of Tuberculous Meningitis, Especially the Tuberculous Arteritis", *The Journal of Experimental Medicine*, Volume I, page 112.

MacGregor, A. R., and Green, C. A. (1937), "Tuberculosis of the Central Nervous System, with Special Reference to Tuberculous Meningitis", *The Journal of Pathology and Bacteriology*, Volume XLV, page 613.

McMurray, James (1944), "Observations on Tuberculous Meningitis", *Archives of Disease in Childhood*, Volume XIX, page 87.

Rich, A. R., and McCordock, H. A. (1933), "The Pathogenesis of Tuberculous Meningitis", *The Bulletin of the Johns Hopkins Hospital*, Volume LII, page 5.

Williams, A. L. (1951), "The Pathology of Tuberculous Meningitis, with Particular Reference to Modification in Pathology following Treatment with Streptomycin", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 680.

PULMONARY TUBERCULOSIS.

The tuberculous children under review as having furnished corroborative cultures of *Mycobacterium tuberculosis* from the gastric content included 17 who were admitted to hospital as suffering from pneumonia, such initial diagnosis having been based on the presence of fever, dyspnœa, and signs detectable by physical examination. Vague ill health, of the nature of lassitude, anorexia and loss of weight, with which cough, sometimes a sequela of measles, was frequently associated, brought under observation 49 other children. With these two groups is to be combined one of 24 apparently healthy children who were subjected to bacteriological examination as household contacts with parents or relatives affected with pulmonary tuberculosis in an active and presumed infective phase. Thus is constituted a group of 90 infants and young children in whom pulmonary manifestations of tuberculous infection predominated.

I do not propose to attempt the inordinately lengthy task of presenting the clinical details of all the children in this group, but rather to comment on the records of selected patients and endeavour to deduce and discuss the precise morbid anatomical processes underlying changes, the distribution and extent of which were revealed by radiography, and the essential nature by bacteriological investigation directed towards the content of the fasting stomach.

Within the compass of this relatively small group of children, only seven of whom died at the Children's Hospital, every vagary of the primary complex was exemplified, from lesions undetectable in lung or lymph nodes by radiography, yet discharging tubercle bacilli which were intercepted in the gastric content, through small pulmonary foci located by a soft and evanescent halo of perifocal exudate, and pneumonic consolidations of lobar dimensions requiring months for their resolution, to a climax reached in a little boy who successfully and with apparent indifference withstood the operation of pneumonectomy; the resected lung had been slowly reduced to a functionless remnant in which extensive caseation and yawning cavitation in the lower lobe were associated with bronchiectasis and a maximum degree of fibrosis throughout the rest of the lung (Figure IV). The phenomenal clinical record of this child was included in a discussion of tuberculous bronchiectasis by Howard Williams (1951). Particularly well illustrated in the series were those dire developments to be laid at the

door of the lymph nodal component of the primary complex, namely, obstructive emphysema, collapse of a pulmonary lobe or segment of a lobe, and residual bronchiectasis.

It is a matter of general recognition that the primary focus, or lesion of entry excited by tubercle bacilli which effect an initial lodgement in the pulmonary parenchyma, is frequently very small and elusive of radiographic detection, and this trite observation was recorded for 14 children whose thoracic radiographs disclosed nothing other than enlargement of the hilar lymph nodes. With respect to the preponderating majority, however, there was no lack of radiographic evidence of disease affecting the pulmonary parenchyma, the reports being accurately descriptive of lesions often surprisingly extensive, even though subsequent developments occasionally proved an "infiltration" the fleeting shadow of a non-specific pneumonitis, or a "consolidation" an atelectasis.

Tuberculous Lobar Pneumonia.

Notable instances of the resolution of tuberculous pneumonia of acute onset and lobar dimensions were observed in two children, represented by the numbers 108 and 117 respectively.

Number 108, a small boy, aged three and a half years, was admitted to the Children's Hospital on January 8, 1950, having suffered from headache, fever, and pain in the right axilla for six days. The report on a thoracic radiograph taken on the day following that of the child's admission to hospital, was an unqualified pronouncement of consolidation affecting the upper lobe of the right lung. The little boy was extremely ill and did not respond to standard treatment, which included injections of penicillin. Streptomycin therapy was instituted and the clinical notes attest that a dramatic effect was observed within twenty-four hours, the temperature falling to normal level.

It was learned that the father of this child was a patient in the Repatriation Hospital, Heidelberg, where he was found to have active pulmonary tuberculosis involving cavitation in the apical portion of the left lung. Incidentally the child was of the fourth generation of his family to suffer from pulmonary tuberculosis. *Mycobacterium tuberculosis* was cultivated from a sample of gastric content withdrawn on January 10 and the child was regarded, properly it would seem, as suffering from acute tuberculous pneumonia. He received in all 24 grammes of streptomycin and was transferred to the Children's Hospital Orthopædic Section, Frankston, where he made extremely satisfactory progress. Radiographs of April 12 and May 15, 1950, showed progressive diminution of the opacity in the upper zone of the right lung, and the radiologist's report of June 16, 1950, six months after the onset of pneumonic illness, stated that clearing of the upper lobe of the right lung had continued and had reached a stage at which the appearance of the lung was almost within normal limits. On August 19, 1950, the child was discharged to the care of his grandparents, a pulmonary lesion, presumably tuberculous, having been discovered by X-ray examination of his mother.

Another story of acute onset of high fever due to extensive pneumonia, which proved very slow in resolution and was proved by gastric mucus culture as tuberculous, is that of number 117, a girl, aged eleven years and ten months. After a period of two months in a private hospital, she was admitted to the Children's Hospital on December 17, 1948, for investigation of a pneumonic consolidation involving the upper lobe of the left lung and refractory to chemotherapy. Although no facts suggestive of tuberculosis could be gleaned from her family history, the girl was found to react strongly to the intradermal injection of 0·1 millilitre of 1 in 1000 dilution of old tuberculin, and *Mycobacterium tuberculosis* was cultivated from a specimen of gastric content secured on December 20, 1948, three days after her admission to the Children's Hospital. The report on a thoracic radiograph of the same date told of extensive deposit in the upper lobe of the left lung, the radiographic appearance being that of consolidation; in addition, opacity was noted in the mid-zone of the right lung. A course of streptomycin therapy was prescribed and the notes record a progressive improvement in the girl's clinical state and in the findings by radiography. From two further specimens of gastric content, of January 26 and March 8, 1949, respectively, *Mycobacterium tuberculosis* could not be cultivated. On her discharge from hospital on July 9, 1949, eight days short of seven months after her admission, the girl looked very well, and her thoracic radiograph was described as showing "very slight residual scarring" in the region of the upper lobe of the left lung.

A baby, aged fifteen months, who figures as number 138 in the series of children from whose gastric content *Mycobacterium tuberculosis* was cultivated, was admitted to hospital on February 2, 1947. He proved a notable example of acute onset of pulmonary tuberculosis of wide progression. He was initially very ill, sustained prolonged high "swinging" fever, and eventually displayed involvement of the whole of the upper lobe, and most of the lower lobe of the left lung in tuberculous consolidation. Despite being called upon to run the gauntlet of measles, chickenpox and several "colds" during his eight and a half months' stay, he left the Children's for the Austin Hospital at the end of this period, afebrile, gaining weight, and clinically very well, his thoracic radiographs having shown progressive clearing.

That tuberculous consolidation of lobar dimensions may on occasions resolve is a conception which has been rendered familiar by the case reports of Parsons (1934) and of Spence (1932), and by Arnold Rich's well-documented advocacy of pneumonic consolidation as a basis for that clinical and radiological phenomenon connoted by the misleading term "epituberculosis". The acute onset and clinical aspect of serious illness exhibited by the three children whom I have cited are features which place them in antithetic relationship with the subjects of "epituberculosis", of the essence of which condition is a state of well-being difficult to reconcile with the extensive, not to say alarming, radiographic shadows which they exhibit. The children whose case records I have briefly presented suffered an illness the onset and clinical features of which were suggestive of lobar pneumonia as incited most typically by pneumococci. Nevertheless the process was proved tuberculous, and three instances of the resolution of an acute tuberculous pneumonia, clinically much more menacing than the benign and frequently unheralded advent of epituberculosis, were notable occurrences, and as such are recorded.

Pulmonary Collapse.

Analysis of the clinical records and radiological reports relating to this series of children showed that the basis for the majority of the larger radiographic shadows, in terms of pathological anatomy, was pulmonary collapse rather than exudative consolidation or pleural exudate. Collapse was sometimes accurately described as such in the reports on the radiographs, but in many instances the radiological criteria of pulmonary collapse were not discernible, and an opacity interpreted as indicative of consolidation was eventually revealed as the silhouette of an atelectatic pulmonary lobe or segment thereof. Caffey (1950) emphasizes that the radiograms of what he terms "tuberculogenic atelectasis" frequently show surprisingly little displacement of the heart and other mediastinal structures, and attributes this observation to filling of the space created by the atelectasis by expansion of the balance of unaffected lung tissue on the same side. The experience of Graham and Hutchison (1947), who found radiographic evidence of mediastinal and/or tracheal shift to the affected side in only 17 of 45 cases of absorption collapse in primary tuberculous pulmonary infection in childhood, is in agreement with this statement. Collapse of a pulmonary lobe or part of a lobe was noted and described in specific terms in the routine thoracic radiographs of 13 children in a total of 54 whose radiographic shadows were of a character which called for decision between collapse and consolidation. Of the 54 children, 41 presented with clinical features of pulmonary disease, and 13 were apparently healthy, their tuberculosis having been detected by routine examination of familial contacts or by school survey, and confirmed by the recovery of *Mycobacterium tuberculosis* from the gastric content. Pulmonary collapse figured, correctly as proved by later developments, in the reports on the standard radiographs, without benefit of tomography or bronchography, in four of the 13 children in the "contact" and apparently healthy group.

That pulmonary collapse occurs much more frequently than routine radiographs suggest is indicated by the fact that, working in the field of research provided by the same children, Howard Williams (1952), my colleague in the Mary and Evelyn Burton Research Foundation, demonstrated, by means of bronchoscopic studies, absorption collapse, its mode of origin and its sequelæ in 32 of 40

children whom he selected for investigation. In 24 of 90 cultures of *Mycobacterium tuberculosis* yielded by gastric content, withdrawn from as many children in whom the clinical or radiological expression of tuberculous infection was pulmonary disease, the morbid process from which such cultures derived was dominated by pulmonary collapse.

Bronchial Stenosis.

In a preliminary report Williams (1951) has ably shown how pathological change, of the nature of bronchial stenosis or occlusion, obstructive emphysema, atelectasis and residual bronchiectasis, may be elucidated in the living by the coordinated application of bronchoscopy and radiography to children suffering from a progressive primary tuberculous infection of the lung. With the exception of those relatively infrequent instances in which the primary focus in the lung parenchyma itself encroaches on a bronchus of sufficient size, the sequence of changes enumerated is to be debited to the lymph nodal component of the primary complex, which is prone to assume predominance, to involve a much greater extent of tissue than the primary focus itself, and to remain unresolved for an indefinite period after the initial lesion in the periphery of the lung has cicatrized. Many are the potentialities for evil vested in caseous hilar lymph nodes; they may transmit tubercle bacilli to the blood stream by way of the thoracic duct or an eroded vessel; as they mass and induce plastic inflammatory changes in the mediastinum they may induce cough and "asthmatoid" symptoms such as stridor and wheezing dyspnœa, particularly in infancy; a contiguous broncho-pulmonary lymph node may erode a bronchus and by the discharge of its content into the lumen induce aspiration tuberculous pneumonia; or in slower and less dramatic manner an enlarged and caseating lymph node may gradually reduce the lumen of a bronchus to a degree upon which the effects of bronchial obstruction supervene. The point from which the sequence of changes which may culminate in bronchiectasis takes origin is that at which bronchial occlusion is established, whether by distortion of the lumen by the pressure or traction of an enlarged caseous lymph node in contact with a bronchus, or by the discharge of caseous matter into the lumen of a bronchus, with consequent endobronchial tuberculosis and aggravation of the bronchial stenosis by the intrusion into the lumen of tuberculous granulation tissue.

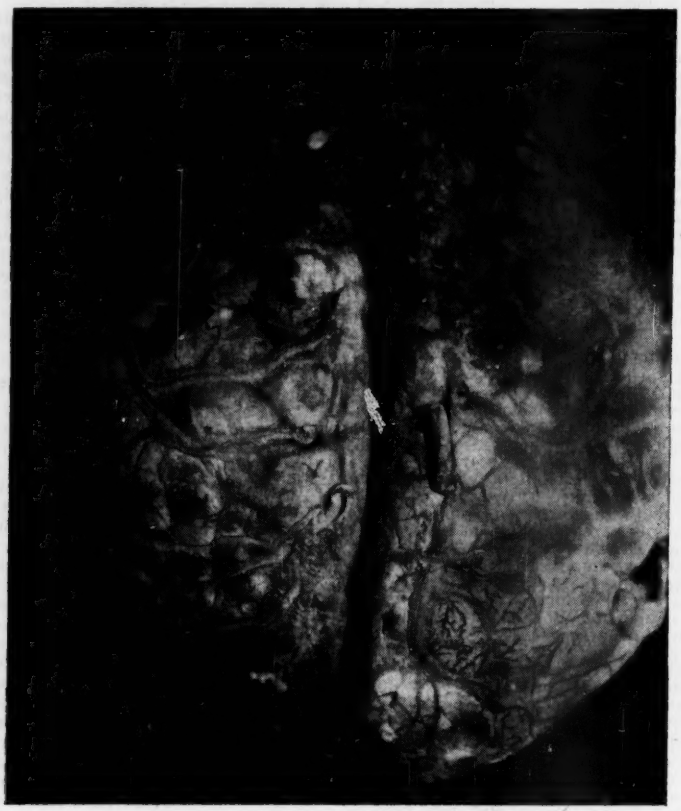

FIGURE III.

Caseous foci in meninges: erosion of pial veins leading to subarachnoid hæmorrhage and visceral miliary tuberculosis: no diffuse meningitis.

The first of the sequelæ of bronchial stenosis or obstruction is emphysema in the lung field served by the affected bronchus—the so-called obstructive emphysema. Such emphysema is most strikingly manifest when its basis is a ball-valve obstruction incidental to the presence of a pedunculated and movable endobronchial tumour, or perhaps a foreign body. But an anatomical ball-valve mechanism is not essential to the production of obstructive emphysema, and such an effect may be brought about by more static stenosing agencies. Under normal conditions inspiration involves a high pressure difference for a relatively short period of time, and expiration a lower pressure difference acting for a longer period of time. The reduced pressure of expiration may not be sufficient to overcome the aggravation of the normal expiratory reduction in lumen of the bronchus by a pathological occluding factor, and retention of air within the pulmonary alveoli gradually builds up the state of obstructive emphysema.

The second stage in the march of events, should the bronchial stenosis advance to more or less complete occlusion, is collapse or atelectasis of a pulmonary lobe or part of a lobe, according as the occlusion affects a major bronchus or one of the second or third order. With the occurrence of atelectasis the stage is set for the development of bronchiectasis, unless such atelectasis is a simple resorption phenomenon, brought about by pressure on the bronchus of an enlarged and contiguous lymph node, attended by no involvement of the bronchial wall in any specifically tuberculous process, and reversible with the reventilation of the lung which follows recession of the obturating lymph node. Unfortunately the process is often far from being readily reversible, as when caseous material remains within the bronchial lumen as a plug, or when, as the result of tuberculous infection of the bronchial mucous membrane, granulation tissue arises to encroach further upon the lumen of the bronchus.

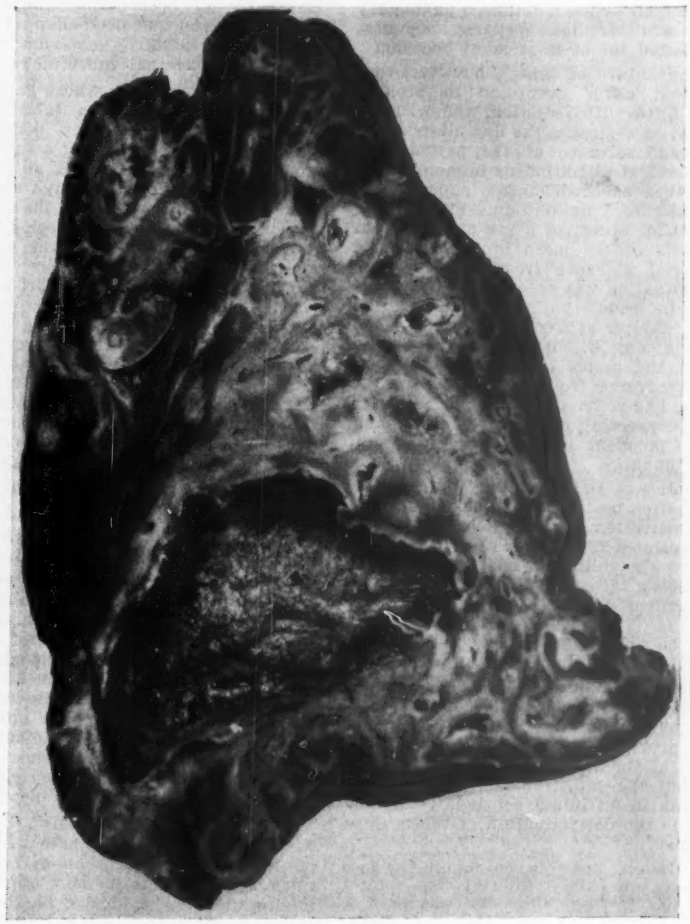

FIGURE IV.

Unique development of primary tuberculous infection of lung: yawning cavitation: exceptional degree of fibrosis: tuberculous bronchiectasis: successful pneumonectomy. Boy, aged five years. By courtesy of the Melbourne University Press.

Tuberculous Bronchiectasis.

The vulnerability of an atelectatic pulmonary lobe or lobule to bronchiectatic change is a matter of common recognition and is intimately involved with the changed mechanical equilibrium of the collapsed pulmonary tissue. The atelectatic portion of lung is airless and respiration effects no change in its volume—it has lost its plasticity and is relatively stiff. Under normal conditions the bronchus is embedded in air-filled yielding pulmonary parenchyma, which takes over the distension occasioned by inspiratory dilatation of the chest; the bronchus may be said to be cushioned against all but a small fraction of the pull of inspiration. If a bronchus is surrounded by atelectatic lung, then the stress and strain of the expanding chest are transmitted directly to the bronchial wall, the traction being unmitigated by the intervention of any yielding or accommodating medium.

The development of bronchiectasis in the evolution of a progressive primary complex may therefore be conceived as proceeding in the following manner. By diminution in the respiratory efficiency of a pulmonary lobe or segment of a lobe, the ability to get rid of secretion is impaired, and the affected lung suffers a depreciation, even a loss, of its self-cleansing power. When the interference with respiratory function is extreme, amounting to abolition, as in atelectasis induced by closure of the lumen of a larger bronchus, to retention of secretion are added loss of plasticity, stiffening and immobility of the collapsed lung, with consequent abnormal pull on the bronchial walls and

ensuing expansion of the branches of the affected segment of the bronchial tree. The dilatation is at first reversible, but becomes permanent if the pathological processes contributing to its inception do not soon resolve. Pyogenic infection might be expected to supervene in bronchi abnormally dilated and filled with mucus, but Williams (1951) emphasized that most children in whom bronchiectasis had evolved in the course of primary tuberculous infection of the lung remained symptomless and well. Graham and Hutchison (1947) described the bronchiectasis which supervened on the tuberculous primary complex in four children while under observation as extensive but "outstandingly free from signs of secondary infection", and recorded their impression that bronchiectasis, when it followed pulmonary collapse deriving from a tuberculous primary complex, seemed to remain uninfected for at least many months.

It would not be in the nature of things, however, that pyogenic infection should never eventuate in bronchi abnormally dilated and filled with secretion, and with its advent there must follow, as the night the day, destruction of the bronchial wall and advance of the pathological state beyond that of bronchial dilatation or bronchiectasis to a phase better described as bronchogenic suppuration. In one of the patients discussed by Williams (1951) such a development ensued on an attack of acute pneumona in a child in whom stenosis of the main bronchus of the right lung was considered a legacy from a tuberculous primary complex. The situation was successfully overcome by surgical removal of the middle and lower lobes of the right lung. As another example of purulent bronchiectasis with a tuberculous basis may be cited the patient who provided number 82 in the series of cultures of *Mycobacterium tuberculosis* recovered from gastric content. A girl, aged nine years, she had suffered from cough, attended by abundant purulent expectoration for five years, and these clinical features of purulent bronchiectasis were supported by radiographic findings.

The bronchoscopic studies of Dr. Howard Williams have involved the necessity for bacteriological examinations directed towards the cultivation of *Mycobacterium tuberculosis* from material aspirated from the lumina of bronchi. The bronchial mucus of six children yielded cultures of *Mycobacterium tuberculosis* after repeated attempts to recover this microorganism from gastric content had proved unsuccessful. It is reasonable to expect that tubercle bacilli should be more susceptible of cultivation at the source of their discharge than at the end of a long migration and subsequent dispersal in the gastric content.

The succession of children in whom pulmonary tuberculosis pursued a course leading to atelectasis and consequent bronchiectasis provided few opportunities for the objective demonstration of the sequence of events by post-mortem examination, but the catastrophe of acute tuberculous bronchopneumonia in an infant represented by the number 11 made possible the determination of tuberculous bronchiectasis by autopsy.

The patient was an infant, aged eleven months, whose mother was known to have entered a sanatorium as a subject of active pulmonary tuberculosis. The baby was said to have been well until he suffered from an attack of bronchopneumonia seven months prior to his admission to the Children's Hospital. A residue of this illness was a cough, which became aggravated two weeks before the infant was brought to hospital, languid and feverish. The radiological report was one of consolidation outlying from the hilum of the right lung and a suggestion of pleural thickening. *Mycobacterium tuberculosis* was cultivated from a sample of the fasting stomach contents withdrawn during the baby's brief stay in hospital. Four days after admission he died.

The autopsy findings relevant to the present discussion were total collapse of the middle lobe of the right lung, which was firmly bound to the upper and lower lobes by pleural adhesions, and the presence of a large caseating tuberculous lymph node, so situated as to reduce greatly the lumen of the main bronchus serving the collapsed lobe by extrinsic pressure. From the dark colour of the middle lobe, its rigidity noted by palpation, and the character of the enveloping pleural adhesions, it was evident that the morbid process was of some duration and it seemed more than probable that it was initiated at the time of the "bronchopneumonia" recorded in the clinical history as having occurred seven months before the child's death. Section of the atelectatic lobe disclosed a congeries of thickened dilated bronchioles, from the lumina of which caseous material was expressed; numerous tubercle bacilli were found in a smear preparation of such detritus.

The autopsy record makes no mention of an existing perforation of the bronchial wall, but the condition of the atelectatic lobe as described rendered inescapable the conclusion that there had been a discharge of the content of the caseated lymph node into the bronchial lumen, with aggravation of the bronchial occlusion, and ensuing aspiration of tubercle bacilli. It was evident also that since this event some degree of restoration of the calibre of the bronchus had been effected, for at autopsy, though striking, the degree of bronchial stenosis fell short of absolute obstruction, and sufficient channel remained to permit the expulsion of infective material, the aspiration of which induced the terminal tuberculous bronchopneumonia.

In the case of a baby whose gastric content provided the culture of *Mycobacterium tuberculosis* number 9, death from tuberculous meningitis permitted the determination by autopsy of the rupture of a tuberculous abscess into the œsophagus. The small cold abscess was the outcome of caseous disintegration of lymph nodes situated in the angle formed by the bifurcation of the trachea, and its discharge was effected through the anterior wall of the œsophagus—an unusual diversion from the course leading to the air passages generally followed by caseous material breaking the bounds of tuberculous broncho-pulmonary or mediastinal lymph nodes. It is on record in medico-legal annals (1885) that the sudden flooding of the trachea and major bronchi with pus deriving from caseous and softened tuberculous mediastinal lymph nodes determined the death of a girl, aged twelve years, from acute asphyxia, and R. B. Scobie (1934), in reporting the recovery of a child from acute asphyxia precipitated in the same manner, included a wide review of the cognate literature, from which he ascertained that 94 such catastrophes had been described and that only 19 of the subjects thereof had recovered.

Epituberculosis.

None of the children under consideration conformed strictly to that radiologically alarming but clinically benign condition known as epituberculosis, cardinal features of which are comparative well-being on the part of the patient and total disappearance of the radiographic shadow; but the favourable course and the degree of radiolucency attained by many in whom the substance behind the shadows was shown by Dr. Howard Williams to be atelectasis, support the view that epituberculosis is very frequently the clinical and radiological expression of pulmonary collapse, the difference between "standard" epituberculosis and the condition elucidated by Dr. Williams in some of these children being one of degree only.

The term "epituberculosis", devised by Eliasberg and Neuland in 1920 to designate what they conceived to be a non-specific exudate prone to occur in the vicinity of a tuberculous process, is now outmoded, inappropriate, and misleading, for evidence has accumulated to establish epituberculosis so-called as a specifically tuberculous process. That the basis is sometimes an extensive pneumonic consolidation capable of resolution though tuberculous, seems to have been irrefutably established by the morbid anatomical studies of Rich (1946), the clinical demonstrations of Spence (1932) and of Parsons (1934), the histological studies of Rubenstein (1928), and of MacGregor and Alexander (1937), and the experimental and histological evidence of Oppenheimer (1935). But another and apparently equally unassailable conception of what he terms the "anatomical substrate" of epituberculosis is that strongly advocated by Terplan (1940), who maintains that atelectasis of a lobe or part of a lobe of the lung, an effect of the impingement of enlarged and caseating lymph nodes on bronchi, is the essential underlying change. Actual perforation of a bronchus, to the wall of which a caseating and softening lymph node has become adherent, may be expected to lead frequently to calamitous endobronchial spread of infection, but it can be understood that should such an erosion of the bronchial wall be effected very

slowly and be followed by a leisurely irruption into the lumen of cheesy matter containing only few viable bacilli, the consequences of the perforation may amount to no more than localized endobronchial tuberculosis, involving of necessity some degree of obstruction of the airway. Terplan describes and reproduces dissections on which he bases his contention that in such circumstances the most impressive effect of the tuberculous process within the bronchus is atelectasis of the corresponding lobe or lobule; he further maintains that the immobility of the collapsed pulmonary tissue operates against aspiration of bacilli, and that if tuberculous lesions occur within the atelectatic zone they are relatively insignificant. Such are the views of Terplan, and they appear to be confirmed by the facts elucidated by Howard Williams's clinical, radiological, and bronchoscopic study of the group of children in whom he demonstrated by these means atelectasis and ensuing bronchiectasis as phases in the evolution of the tuberculous primary complex in the lung. It would appear from the papers of different workers interested in this subject—Graham and Hutchison (1947), Kent (1942)—that the view is steadily gaining ground that "epituberculosis" is in the majority of instances to be regarded as the clinical and radiological expression of atelectasis, rather than resolving pneumonic consolidation. In either event this unsatisfactory term, for which there seems to be no further use, represents not a pathological entity, but the favourable outcome of accidents intimately related to the processes of enlargement, caseation, and softening in the lymph-nodal component of the primary complex.

Familial Contact Group.

The cultivation of *Mycobacterium tuberculosis* from the gastric content of 24 apparently healthy children examined radiographically and bacteriologically as close "contacts" of parents or relatives known to be suffering from pulmonary tuberculosis provided findings for which the morbid anatomical basis was in some instances beyond the range of radiological perception, as against others which excited wonder that a child could support active pulmonary tuberculosis of the extent disclosed by radiography with no obvious deterioration in health.

By common consent small primary lesions, which may possibly not have attained macroscopic size, much less effected the necessary alteration in density of the involved pulmonary parenchyma, are not expected to register in a radiograph, and it might perhaps be anticipated that bacteriological efforts to demonstrate the presence of *Mycobacterium tuberculosis* in such an early phase of its activity are likewise doomed to failure; the size of a lesion, however, is no criterion of the number of bacilli it might be expected to discharge.

There is no theoretical objection to the suggestion that tubercle bacilli, emanating from a pneumonic focus of little more than miliary size, may wend their way, or rather be transported, through minute terminal bronchioles and those of progressively larger calibre, to a point whence they gain access to the outer world in expelled bronchial mucus. The demonstration of tubercle bacilli in the product of gastric lavage, so early in the course of primary infection as to antedate the appearance of tuberculin sensitivity by approximately one week, has been reported by Wallgren (1935), than whom no one writes with greater authority on the subject of tuberculosis in childhood. The patient was a female infant of seven months of age, who had been infected by her mother. At the time of discovery of tubercle bacilli in the gastric washing, no reaction to the injection of "large doses" of tuberculin could be elicited, and the thoracic radiograph was of normal appearance. Wallgren added that similar observations were later reported by Saye and Poulsen.

In a former publication (1947) I have recorded the cultivation of tubercle bacilli from the gastric content of each of three student nurses, who were found to have developed sensitivity to tuberculin in the course of routine testing at three-monthly intervals. Radiological and bacteriological examinations carried out within a few days of the discovery of tuberculin sensitivity resulted in each instance in the cultivation of *Mycobacterium tuberculosis* from the gastric mucus despite the lack of radiographic evidence of any pathological process in the lungs. The observation has since been repeated in each of two other nurses and the present review of cultures of *Mycobacterium tuberculosis* which I have obtained from the gastric content of children brings it to the fore again.

A case in point is that of a child (number 159), aged four and a half years, who was admitted to hospital for a vague and, as it proved, transient indisposition, on December 15, 1951. By reason of the fact that his father had been determined as tuberculous four months previously, a sample of the content of the fasting stomach, from which *Mycobacterium tuberculosis* was in due course recovered, was withdrawn on December 20. The boy was discharged apparently well on the following day, having occupied a bed for one week, during which interval a thoracic radiograph was reported as "clear".

Of particular interest in the same sense was another little boy, number 148. He was six years of age and presented on January 26, 1950. His mother had recently been discharged from a sanatorium. He was found to be tuberculin-sensitive and displayed phlyctenular conjunctivitis as an additional suggestive feature. *Mycobacterium tuberculosis* appeared in cultures prepared from a specimen of gastric content withdrawn on February 2, one week later than the issue of a report on a thoracic radiograph, which read: "Triangular opacity at left base posteriorly, suggesting pneumonitis or segmental collapse. No specific evidence of tuberculosis."

The terminal comment in this report was well advised, for specific evidence of tuberculosis cannot be read in a radiographic shadow; a recent primary complex exhibits no pathognomonic features discernible by radiography, and lobar and lobular consolidations due to intraalveolar exudate excited by such microorganisms as pneumococci and streptococci are not to be distinguished from those of tuberculous nature by the shadows they cast. Even apparently characteristic miliary stippling may be referable to causes other than tuberculosis, and I have known a radiograph identified as one of miliary tuberculosis prove to have been a record in silhouette of innumerable small metastases in the lungs from a cystic papillary adenocarcinoma of the thyroid—the so-called "lateral aberrant thyroid".

Whatever the basis for the opacity noted in the first thoracic radiograph of this boy, it was found to have dissipated in a second radiograph taken two months later, on March 20, 1950, and thereafter four consecutive radiographs, secured in the course of a ten-months period marked by the date January 15, 1951, were pronounced free from blemish. Two of the serial radiographs in which no flaw could be detected in either lung fields or hilar regions, were taken on October 2 and 26, 1950, respectively; during that month *Mycobacterium tuberculosis* was again cultivated from the boy's gastric content, eight months after the first occasion of its recovery. At the end of twelve months tubercle bacilli could no longer be cultivated from the gastric mucus.

It is possible that the evanescent shadow observed in the first radiograph was cast by a perifocal exudate enveloping a small primary lesion, which remained radioinvisible after its smoke screen had dispersed. At all events tubercle bacilli were demonstrated in the gastric content by cultivation, eight months after their detection by similar means in the first instance, and during this period the child had exhibited neither clinical nor radiographic signs of pulmonary tuberculosis. That the tubercle bacilli detected in the gastric content were of faucial origin, the child harbouring *Mycobacterium tuberculosis* in the pharyngeal lymphoid tissue in the capacity of "carrier", is a theoretical possibility. Most writers on the subject do not accept the concept of tubercle bacillus "carrier" in the strict sense of the term, and consider rather that patients concerning whom such question arises are subjects of occult tuberculosis. Floyd and Novack (1931) subscribed to the definition of "carriers" of tubercle bacilli as individuals harbouring microorganisms, virulent or avirulent, but not suffering from the concomitant disease. They recorded notes of four patients in whom positive findings with respect to tubercle bacilli in the sputum were obtained concurrently with radiographs affording no evidence of pulmonary disease, and estimated the incidence

of such a situation as one in approximately 10,000 cases. This figure, based on the findings obtained by the inadequate technique of microscopic examination of smears of sputum, I would dismiss as patently an under-statement of the frequency with which tubercle bacilli may be demonstrated in persons whose health appears clinically flawless and who are radiologically irreproachable. Experience in the cultivation of tubercle bacilli from sputum and gastric content of army recruits, trainee nurses, and "contact" children has convinced me that the seeming paradox of positive bacteriological findings in the absence of clinical and radiological evidence of tuberculosis arises much more often than once in 10,000 times. Individuals in whom investigation leads to such results are less likely to be "carriers" of tubercle bacilli, in the sense in which this term is applied to human vectors of typhoid and dysentery bacilli, than subjects of a cryptic and radiologically undetectable focus of tuberculous disease.

It is improbable, however, that considerations of the carrier state have any application to the case of the boy (number 148) under discussion, his home environment, reactivity to the Mantoux test, and phlyctenular conjunctivitis combining in a triad of evidential points indicative of the existence of an obscurely located tuberculous lesion.

Failure to locate a primary tuberculous lesion in the pulmonary parenchyma by radiography was experienced with respect to seven other children, but the negative character of the radiological reports in this particular was in each instance tempered by the observation of enlargement of the hilar lymph nodes. Any pulmonary infective process is prone to be reflected in the mediastinal lymph nodes, and even though tuberculous hilar adenopathy was implicit in the fact of household contact with infective pulmonary tuberculosis established for these children, the cultivation of *Mycobacterium tuberculosis* was desirable and necessary for indubitable diagnosis. Radiographic observation of enlarged hilar lymph nodes, eventually proved tuberculous, unaccompanied by any detectable primary lesion in the lung, serves but to emphasize the fact that the tuberculous primary complex, wherever it may be initiated, be it in the lung, tonsil, intestinal mucosa, the skin by inoculation, or even the conjunctiva, is prone to be dominated by the lymph-nodal component; in the mediastinum particularly, lymph nodes contributing to a primary complex are responsible for many evils of local and metastatic spread.

Calcification in the hilar and paratracheal lymph nodes was noted in the case of a boy (number 112), aged two years, in whose mother pulmonary tuberculosis was discovered when she was nursing the child, then aged six months. The boy was apparently well and to the X-ray record of calcification in the mediastinal lymph nodes was added a note that no peripheral or fresh deposit was detectable. At the time, his elder sister, affected with pulmonary tuberculosis, was a patient in the Austin Hospital. That the hilar lymph adenopathy was essentially tuberculous could not reasonably be doubted, and despite the lack of an identifiable primary focus and the suggestion of inactivity conveyed by the radiographic appearance of the hilar lymph nodes, *Mycobacterium tuberculosis* was cultivated from the gastric mucus.

It would seem appropriate at this point to observe that calcification, of itself, is not conclusive evidence of tuberculosis, occurring as it does in the sites and products of old inflammatory processes, those of pyogenic, tuberculous, syphilitic and mycotic origin, and supervening on the retrogression of parasitic cysts, as on necrosis in malignant neoplasms. But in this country, where, to the best of my knowledge, histoplasmosis does not intrude nor coccidiomycosis confuse the issue, calcification in the pulmonary parenchyma of hilar lymph nodes is to be assigned to tuberculosis much more frequently than to any other cause.

In two of the "contact" children, number 2 and number 149, progress of the primary focus in the lung permitted its detection in radiographs taken five and seven weeks respectively after those in which hilar adenopathy alone was discerned.

Active pulmonary tuberculosis, unaccompanied by any appreciable departure from normal health, was revealed in a little girl (number 77), aged four and a half years, for whom investigation was instituted solely on account of the presence in the home of her tuberculous father. The report on the radiograph described as "...dive" a lesion infiltrating upwards from the perihilar region of the right lung. The radiographic assessment of activity was confirmed by the cultivation of *Mycobacterium tuberculosis* from the gastric content on the first attempt.

A very similar story is that of a little girl, aged three years (number 101), who was referred to the Children's Hospital from the Central Tuberculosis Bureau as having lived in household contact with her adult stepsister, a subject of pulmonary tuberculosis awaiting admission to a sanatorium. An active child and full of energy, her radiograph of September 18, 1950, revealed consolidation in the upper lobe of the right lung, accompanied by peribronchial and paratracheal glandular enlargement. Two months later *Mycobacterium tuberculosis* was still recoverable by cultivation from the gastric content. In much the same language could be stated the clinical, radiological, and bacteriological facts concerning five other children, in whom pulmonary tuberculosis, by no means inactive, was unveiled by the routine examination of contacts, but the findings in the case of a baby of eleven months (number 124) were truly remarkable.

In the course of an examination of her family, the members of which had been living in contact with a subject of "open" pulmonary tuberculosis, a radiograph taken at the Central Tuberculosis Bureau on February 24, 1948, disclosed a widespread mottling, very suggestive of miliary tuberculosis, throughout the greater part of both lungs, and this in an infant who appeared well and was gaining weight! The radiographic findings were confirmed at the Children's Hospital on March 31, 1948, and the soft diffuse mottling was found persisting on April 20, with the added radiographic features of patches of confluence at the bases of both lungs. In the meantime *Mycobacterium tuberculosis* had been cultivated from the child's gastric content. Streptomycin therapy was instituted on April 23 and continued until June 20, 1948.

On May 6 a little clearing of the lung fields was noted radiographically, and advance in this direction was recorded on July 8, though there was still a notable degree of feathery opacity radiating from both hilar regions towards the bases of the lungs. Stippled opacities discernible in the right lateral view were suggestive of calcification in an early stage. Five weeks later the mottling was described as reticulated, with a linear rather than a discrete character. The infant was discharged to the thoracic unit of the out-patient department on August 21, 1948, after nearly five months in hospital, as "a really lovely fat baby girl whose miliary tuberculosis appeared to have been arrested by streptomycin" (clinical record). Surely a unique episide in the routine examination of contacts! A recent inquiry directed by letter to the child's parents, after the lapse of four years, brought the reply that she was very well.

Six of the children investigated as having lived in a tuberculous environment eventually found their way to the Clinical Research Unit, directed by Dr. Howard Williams, and provided material for his bronchoscopic studies. The varying degrees of pulmonary collapse and residual bronchiectasis with which these and other patients were ultimately found to be affected are to be described and discussed by Williams (1952), who in an earlier report (1951) emphasized the frequently silent onset of pulmonary collapse and insidious development of tuberculous bronchiectasis.

References.

Annotation (1885), *The Lancet*, Volume II, page 395.

Caffey, J. (1950), "Pædiatric X Ray Diagnosis", Second Edition, The Year Book Publishers, Incorporated.

Floyd, C., and Novack, H. (1931), "The Carrier of Tubercle Bacilli", *The New England Journal of Medicine*, Volume CCIV, page 543.

Graham, S., and Hutchison, J. H. (1947), "Absorption Collapse in Primary Tuberculous Infection in Childhood", *Archives of Disease in Childhood*, Volume XXII, page 162.

Kent, E. M. (1942), "Bronchial Obstruction and Pulmonary Atelectasis: As Seen in Childhood Tuberculosis with Secondary Bronchiectasis as a Sequela", *The American Review of Tuberculosis*, Volume XLVI, page 524.

MacGregor, A., and Alexander, W. A. (1937), "Pulmonary Tuberculosis in Children", *Edinburgh Medical Journal*, Volume XLIV, page 561.

Oppenheimer, E. H. (1935), "Experimental Studies on the Pathogenesis of Tuberculosis", *The Bulletin of the Johns Hopkins Hospital*, Volume LVII, page 247.
Parsons, L. G. (1934), "The Childhood Type of Tuberculosis", *The Lancet*, Volume I, page 1101.
Rich, A. R. (1946), "The Pathogenesis of Tuberculosis", pages 837 *et sequentes*, Charles C. Thomas, Springfield, Illinois.
Rubenstein, H. (1928), cited by A. R. Rich, *loco citato*, page 834.
Scobie, R. B. (1934), "Acute Asphyxia from Intrabronchial Rupture of Tuberculous Mediastinal Gland with Recovery", *The American Journal of Diseases of Children*, Volume XLVIII, page 373.
Spence, J. C. (1932), "Benign Tuberculous Infiltration of the Lung (Epituberculosis)", *Archives of Disease in Childhood*, Volume VII, page 1.
Terplan, K. (1940), "Anatomical Studies on Human Tuberculosis", *The American Review of Tuberculosis* (Supplement), Volume XLII, page 63.
Wallgren, A. (1935), "Primary Tuberculosis in Childhood", *American Journal of Diseases of Children*, Volume XLIX, page 1105.
Webster, R. (1947), "Mathison Memorial Lecture", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 605.
Williams, H. E. (1951), "Bronchiectasis following Primary Tuberculous Infection in Children", report of meeting of the Melbourne Pædiatric Society, THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 238.
——— (1952), personal communication.

HÆMOPTYSIS.

Hæmoptysis seldom occurs as a symptom of pulmonary tuberculosis in childhood, but this untoward event figures in the clinical records of three children in whom the essential ætiological factor was established by cultivation of tubercle bacilli from the gastric content. The recovery of *Mycobacterium tuberculosis*, however, threw no light on the precise nature of the underlying morbid process, and was of no assistance in estimating whether the hæmoptysis was a concomitant of primary infection or was an incident in the course of pulmonary tuberculosis of reinoculation or so-called "adult" type. That the latter view is the more probable with respect to the child represented by the number 111 is suggested by the clinical facts and radiological findings concerning her.

The patient was a girl, aged ten years, said to have been well until a brisk hæmoptysis determined her admission to the Children's Hospital in October, 1949. A disease process attended by cavitation, and situated in the upper lobe of the right lung, was disclosed by a thoracic radiograph and the cavity clearly defined by tomographs. The girl had been in frequent contact with a tuberculous aunt, her reaction to the Mantoux test progressed to vesiculation, and the growth of *Mycobacterium tuberculosis* from the gastric mucus was rapid and profuse. Five months later tubercle bacilli were still recoverable from the gastric reservoir, but in July, 1950, nine months after the initial hæmoptysis, an attempt at cultivation of *Mycobacterium tuberculosis* from this source failed. In the meantime the girl had received a course of 20 milligrammes of streptomycin and was considered clinically to have made good progress.

The abrupt onset of the hæmoptysis and the clarity with which cavitation in the upper lobe of the right lung was demonstrated convey a strong impression that the hæmorrhage originated from the rupture of an unsupported blood vessel traversing the apical cavity, in a manner rarely witnessed in childhood, but of too common occurrence in adults.

The second of the three patients whose admission to the Children's Hospital was occasioned by hæmoptysis and from whose gastric content *Mycobacterium tuberculosis* was cultivated, was a boy (number 119), aged five years, admitted on November 16, 1948. Radiographs of the chest taken in November, 1948, and in February, 1949, were passed as showing no pulmonary or hilar lymph node abnormality. By bronchoscopic examination on February 11, 1949, Dr. Howard Williams was unable to demonstrate any lesion to which the hæmoptysis might be referred. The boy was well at this time and the source of the hæmoptysis and of the tubercle bacilli cultivated from his gastric content remained obscure.

An explanation of the clinical fact of hæmoptysis and of the laboratory finding of tubercle bacilli in the gastric content in the case of this boy would seem to lie in regarding him as providing another example of the failure of radiography to locate a small primary lesion, and in postulating the erosion of a tiny vessel in the caseation and softening incidental to such a focus, small as it may have been.

The clinical and radiological features presented by the third child in this group (number 134), despite the fact that her age was only five years and two months, suggest that her illness may be legitimately regarded as pulmonary tuberculosis of reinoculation or "adult" type. The child first attended the Children's Hospital in 1944; she was then aged three years, and the death of her mother from pulmonary tuberculosis in 1942 was the indication for a tuberculin test and a radiograph of the chest. The little girl was found to react to 0·1 millilitre of 1 in 1000 dilution of old tuberculin injected intradermally, but the thoracic radiograph was passed as "clear". The inference drawn was that the child had sustained a primary tuberculous infection which she had successfully withstood.

Hæmoptysis and fever were the precipitating factors in the child's reappearance two years later, on September 3, 1946. A thoracic radiograph of that date disclosed exaggerated hilar markings on the right side, and peribronchial thickening in the upper lobes of both lungs, more conspicuous in the right lung than in the left. Three months later a soft diffuse opacity was apparent in the upper lobe of the right lung, and on the left side nodular infiltration at the levels of the second and third intercostal spaces was observed.

A radiograph taken after the lapse of a further three months — March 18, 1947 — was interpreted as showing broadening of the diffuse mottled shadow in the upper lobe of the right lung. *Mycobacterium tuberculosis* was cultivated from a sample of the child's gastric mucus withdrawn a day or two after she presented in September, 1946, and was still recoverable from this source in April, 1947. Despite the radiological and bacteriological findings, the child was happy and apparently well.

An illness initiated by hæmoptysis and fever two years after the demonstration of tuberculin sensitivity, underlying which no focus of pulmonary disease could be detected radiographically at the time, and exhibiting a progressive apical pulmonary lesion confirmed bacteriologically as tuberculous, seems to conform to the pattern of the reinoculation or "adult" type of pulmonary tuberculosis. The early age of five years does not exclude such a view. At the same time consideration is due to the possibility of the reactivation and advance of a quiescent focus of primary infection, present but undisclosed at the time of the X-ray examination to which the child was submitted in 1944 as a familial "contact" with infective pulmonary tuberculosis.

The terms "childhood type" and "adult type", as applied to pulmonary tuberculosis, maintain themselves tenaciously in the literature of the subject, but it has long been evident that the distinction is artificial. Primary infection, with its non-selective localization in the lung, its predominance of caseation, lack of fibrosis, and conspicuous and early involvement of lymph nodes, is displayed most typically, but by no means exclusively, in the child; the lesions consequent on reinoculation, distinguished by predilection for the upper lobes, fibrosis, a reduced propensity to caseation, and greatly diminished tendency to involve regional lymph nodes, are generally, but not invariably, deferred until adult life. It would be superfluous to labour the liability of young adults to primary infection, an event which undoubtedly occurs more frequently than its counterpart, reinoculation in childhood. Chronic fibroid pulmonary tuberculosis of reinoculation type is not, however, a rarity in older children, and observation of an example in a child so young as three years is mentioned by Holt and McIntosh (1940).

Reference.

Holt, L. E., and McIntosh, R. (1940), "Holt's Diseases of Infancy and Childhood", Eleventh Edition, page 1301, Appleton-Century-Crofts, Incorporated, New York.

PLEURISY WITH EFFUSION.

In ten of the children whose gastric content yielded *Mycobacterium tuberculosis* in culture, the presenting and dominant clinical feature was pleurisy with effusion. The ages of the patients conformed to rule in that infants and toddlers were not represented; the youngest child in the group was six years of age, and three had attained double figures. In infants and very young children pleurisy with effusion is an unusual manifestation of primary tuberculous infection, but that the possibility of its occurrence at a very early age cannot be discounted, is evident from Hardy

and Kendig's communication (1945) relating to pleurisy with effusion as observed in 13 of 393 (3·3%) tuberculous children under the age of two years.

The manner of development of tuberculous pleurisy, the common but not inevitable clinical expression of which is an effusion of serous fluid into the pleural sac, is not far to seek, the clue being provided by the predilection of the initially small lesion of entry of tubercle bacilli in the pulmonary parenchyma—the Ghon focus—for a peripheral situation which, if it does not abut on the pleura, is seldom far from it. A relatively small extension of a caseating and softening primary lesion suffices to implicate the overlying pleura, and ensuing erosion of the serous membrane permits the entry of tubercle bacilli into the pleural sac. One or other of the lymph nodal components of the primary complex may similarly involve the pleura at a point in the mediastinal reflection of this membrane, disrupt its integrity, and discharge caseous matter carrying tubercle bacilli and impregnated with the products of their disintegration into the pleural cavity. Irruption of the content of a caseating lymph node into the lumen of a bronchus is a well-substantiated observation, and it may well be that on occasions the way to the pleural cavity proves the path of less resistance.

In nine of the ten children in whom the presumptive diagnosis of tuberculous pleurisy with effusion was confirmed by the cultivation of *Mycobacterium tuberculosis* from the gastric content, it was not possible to estimate with any degree of probability the interval which elapsed between the establishment of primary infection and the onset of the pleural effusion, but in the tenth, a boy, aged eleven years, the occurrence of *erythema nodosum* provided a basis upon which this period might be computed. *Erythema nodosum* as a manifestation of primary tuberculous infection is generally believed to fix the actual date of infection as lying between sixty and thirty days before the appearance of the nodular eruption, and was recorded for this boy on August 6, 1939. Two months later, October 4, 1939, he returned to the Children's Hospital exhibiting an unmistakable pleural effusion. The dates indicate the supervention of tuberculous pleurisy on primary infection after the relatively short interval of not less than three and not more than four months, the latent period being generally considered to be six to twelve months.

Brian C. Thompson (1949) has published, as illuminating the question of the pathogenesis of pleural effusion of tuberculous origin, details of a careful study of seven young adults who were known to have contracted a primary tuberculous infection of recent date and had been under close observation before and after that misadventure. In six of the seven a primary complex within the thorax developed under observation, and in five the initial lesions remained radiographically visible throughout the subsequent pleurisy. Of these favourable conditions for study the author took full advantage. Direct spread from the pulmonary focus to the neighbouring pleura could be read in the radiographs of two of the patients, and the films of three were considered by Thompson to provide strong evidence that the pleura was infected from caseous lymph nodes ensheathed in the pleural covering of the root of the lung.

In the case of the patient represented by the number 4, a boy, aged nine years, a serous effusion occupied both pleural sacs at the time of the recovery of *Mycobacterium tuberculosis* from his gastric content, and such bilateral effusions may reasonably be attributed to a spread of infection to the opposite pleura from adjacent lymph nodes.

It is to be noted with respect to number 28, a girl, aged seven years, that *Mycobacterium tuberculosis* was still recoverable from her gastric content two years and three months after the onset of the pleural effusion which determined her admission to the Children's Hospital on December 12, 1940.

A third member of the group presenting with pleural effusion, number 38, a boy, aged eleven years, died of tuberculous meningitis three weeks after admission to hospital on October 20, 1943, and a few days before the appearance of colonies of *Mycobacterium tuberculosis* in cultures prepared from a sample of the content of the fasting stomach withdrawn within a day or two of his entering the Children's Hospital. At autopsy the left pleural cavity was found totally obliterated, the visceral and parietal layers of the pleura being bound together by adhesions of incredible extent and density, having regard to the fact that three weeks earlier the pleural sac was occupied by serous fluid. So firmly bound to the parietes was the left lung that its removal was a matter of great difficulty, and the process, which was literally one of excavation, involved much laceration of the peripheral pulmonary tissue. As a result, the primary focus, the presence and activity of which were indicated by the cultivation of *Mycobacterium tuberculosis* from the gastric content only three weeks before death, was not identified; it was presumed that it was very small, in close proximity to the pleura, and that it was disintegrated and dispersed by the tearing involved in the difficult process of delivery of the lung. Caseating lymph nodes in the hilum, however, were so situated as to indicate the lower lobe of the left lung as the site of the primary lesion. The absorption of an effusion judged to be of moderate amount and the organization of the deposited fibrin into adhesions of such extent and density within the short interval of three weeks were findings which I viewed with astonishment, which has not abated in any degree during the intervening nine years.

Pathogenesis of Tuberculous Pleurisy.

The situation of most primary tuberculous pulmonary lesions in close proximity to the pleura might suggest that the serous covering of the lung could be involved in an exudative inflammation excited by bacillary disintegration products, such as might be diffused from the neighbouring primary focus, or liberated by a disturbance in the lymph-nodal component of the primary complex, to be conveyed by the blood stream to the site of coexisting active tuberculous disease. This is the familiar focal hypersensitive reaction, originally invoked in explanation of the phenomena of so-called epituberculosis; as a solution to the problem of the essential underlying change in epituberculosis, perifocal exudate is dismissed by Arnold Rich (1946) as having no basis in observation and as contrary to all available information. The reasons advanced by this authority in objection to the focal hypersensitive reaction as the substrate of epituberculosis would seem to apply with equal force to the conception that an exudate of volume equal to that of the average pleural effusion might occur as a focal expression of hypersensitivity. Lest the part played by the hypersensitive state seem to have been underrated let it be added promptly that hypersensitivity of the pleura to the tubercle bacillus and the products of its activity, induced by a tuberculous infection of the lung, usually of several months' standing, is a condition precedent to the large-scale exudative reaction which constitutes the clinical entity tuberculous pleurisy with effusion.

Experimental work by R. C. Paterson (1917) was designed specifically for the elucidation of this point. The worker named showed that the direct inoculation of the pleura with living virulent tubercle bacilli excited in guinea-pigs previously sensitized by the injection of appropriate doses of a strain of *Mycobacterium tuberculosis* of low virulence, an immediate and intense local reaction, of the nature of acute inflammation, and attended by dilatation of vessels, exudation of serum, and deposition of fibrin. This consistent and characteristic reaction did not occur in control animals, in which there was little or no immediate pleural reaction. With excessive doses of infecting tubercle bacilli there might be a small amount of serous fluid exuded in normal animals, but it was invariably less than in the vaccinated animals and did not always occur; smaller doses elicited no exudation from the pleura of the normal, non-sensitized animal.

Direct inoculation of the pleura of rabbits rendered sensitive to tuberculin, and of normal rabbits as controls, was undertaken at a later date by Pinner (1928), with the object of studying the reaction to reinfection in tuberculosis, and particularly the extent to which the productive or exudative phase predominated in such reaction. His well-based criticism of Paterson's widely accepted and oft-quoted work was that it was focused on the exudative feature, to the neglect of the proliferative aspect. As a result the impression propagated was that the reaction to reinfection with tubercle bacilli was exudative only, and that there was in fact a qualitative difference between the reactions to first and subsequent infections in that the productive process, exemplified by the formation of

tubercles, was a negligible consideration in the predominantly exudative reaction to reinfection. With regard to the exaltation of the exudative phase in the reaction to reinfection, Pinner found in agreement with Paterson, but he presented his experimental results as indicating clearly that the exaggeration of the exudative reaction was accompanied by an acceleration of productive processes. There was thus no qualitative difference between the reaction to primary infection and that to reinfection; neither was purely productive or purely exudative.

It seems probable that anatomical conditions favour a free exudation of fluid when the site of reinfection is the pleural serous membrane, but other influences affecting the volume of the effusion are the degree of hypersensitivity attained and the number and virulence of the reinfecting tubercle bacilli. Should all these factors be operative in high degree, a maximum outpouring of fluid might be anticipated; conversely, should a small number of bacilli of relatively low virulence gain access to the pleura of an individual who has not developed a high order of sensitivity, the ensuing reaction might amount to no more than the production of a few tubercles, and the exudation of fibrin-depositing serous fluid in quantity too small to be appreciable clinically as a pleural effusion. The frequently tuberculous nature of "dry" pleurisy is now no longer a subject of contention.

It is inconceivable that sufficient tuberculo-protein can be diffused from the subpleural primary focus or be brought by hæmic carriage from a distant source to bring the mechanism of hypersensitivity into operation on a large scale. Nothing less than the actual entry of living and actively multiplying tubercle bacilli to the pleural sac will evoke the reaction of hypersensitivity with all the potential for exaggerated exudation manifested in tuberculous pleurisy with effusion.

That tubercle bacilli are actively and directly concerned in this natural development in the course of primary tuberculous infection of the lung is shown by the degree of success which has been attained by patient and painstaking workers in the cultivation of *Mycobacterium tuberculosis* from the familiar, straw-coloured serous exudate of tuberculous pleural effusion. My own experience in this regard has been disappointing, but I have seldom received more than 10 to 20 millilitres of fluid, it being the practice at the Children's Hospital to restrict aspiration to diagnostic requirements. The principle of multiple sowings essential to success in the cultivation of *Mycobacterium tuberculosis* from any source has been applied by Close (1946), who by the utilization of deposit and clot from 100 millilitres or more of pleural fluid, and the inoculation therewith of ten or more tubes of Löwenstein-Jensen medium, recovered *Mycobacterium tuberculosis* from the pleural effusions of 16 of 20 patients who came under observation during the first eight months of the year 1945 and were regarded on clinical grounds as tuberculous. Close indicated that in nine of eighteen specimens of pleural fluid colonies of *Mycobacterium tuberculosis* appeared in only one of ten or more appropriately prepared culture tubes, and remarked that the presence of *Mycobacterium tuberculosis* would probably not have been disclosed had the practice of sowing only a few clots or the deposit from a small amount of fluid been followed. It is interesting to observe that this worker found culture medium more effective than the guinea-pig in revealing the presence of tubercle bacilli in pleural effusions.

The origin of tuberculous pleurisy by the discharge of the contents of a caseous focus, pulmonary or lymph-nodal, abutting on the pleural sac brings this essentially post-primary development into line with the conception of the pathogenesis of meningeal tuberculosis vigorously promulgated by Arnold Rich (1933). If the subarachnoid space be regarded as a serous cavity, it may be said that the conditions governing an extensive tuberculous inflammatory effusion in all serous cavities are the same. Experimental injection of tubercle bacilli into the blood stream of either normal or hypersensitive animals has not sufficed to induce an exudative inflammation in the subarachnoid space or in the pleural, pericardial, or peritoneal cavity. The serous membranes are so seldom involved in miliary tuberculosis as to render it improbable that tuberculous pleurisy, occurring in quasi-primary and apparently isolated fashion, is of hæmic origin. Spread of infection from softened caseous lesions in the vicinity is responsible for tuberculous pleurisy, as for tuberculous pericarditis or peritonitis. Neighbouring hilar lymph nodes may menace the pericardium, a perforating ulcer of the bowel, caseous mesenteric lymph nodes, or possibly a tuberculous Fallopian tube, the peritoneum.

References.

Close, H. G. (1946), "Tubercle Bacilli in the Pleural Effusions of Young Adults", *The Lancet*, Volume I, page 193.

Hardy, J. B., and Kendig, E. L. (1945), "Tuberculous Pleural Effusion in Infancy", *Journal of Pædiatrics*, Volume XXVI, page 138.

Paterson, R. C. (1917), "The Pleural Reaction to Inoculation with Tubercle Bacilli in Vaccinated and Normal Guinea-Pigs", *The American Review of Tuberculosis*, Volume I, page 353.

Pinner, Max (1928), "A Note on Exudative and Productive Processes in Pleural Tuberculous Infection", *The American Review of Tuberculosis*, Volume XVII, page 627.

Rich, A. R. (1946), "The Pathogenesis of Tuberculosis", *Charles C. Thomas, Springfield, Illinois*, page 835.

Rich, A. R., and McCordock, H. A. (1933), "The Pathogenesis of Tuberculous Meningitis", *The Bulletin of the Johns Hopkins Hospital*, Volume LII, page 5.

Thompson, B. C. (1949), "Studies in Primary Pleurisy with Effusion", *British Medical Journal*, Volume II, page 801.

Tuberculosis of Bones and Joints.

Cultures of *Mycobacterium tuberculosis* were obtained on one or more occasions from the mucus aspirated from the fasting stomach of each of 15 children who presented with limp or objective clinical manifestations of arthritis. Although in 13 of the 15 children household contact with infective tuberculosis, tuberculin sensitivity, and the presence of radiographic signs consistent with a tuberculous process involving the pulmonary parenchyma, hilar lymph nodes, and/or the affected bone or joint, combined to render the diagnosis of tuberculous arthritis very probable, the recovery of *Mycobacterium tuberculosis* from the gastric content provided the corroborative evidence which eliminated all element of presumption. In the remaining two patients, both boys in whom tuberculosis of the hip joint eventually pursued a relentless and destructive course, diagnosis in the early stage of disability was a very open question.

The first of these patients, a boy, aged six years, who furnished number 17 in the series of cultures of *Mycobacterium tuberculosis*, had been limping for four weeks when he was admitted to the Children's Hospital on November 1, 1940. The limp was attributed to a knock on the hip, the site of the injury being marked by a bruised swelling, which, however, was said to have developed on the day preceding the boy's admission to hospital. Tuberculin sensitivity was elicited by both the Mantoux intradermal and Vollmer "patch" tests, but no familial contact with tuberculosis could be determined. Bacteriological investigation of the gastric content and X-ray examination of the chest were instituted on consecutive days. *Mycobacterium tuberculosis* was readily cultivated from the gastric mucus, and the radiologist noted an exaggerated shadow in the hilum of the left lung, with associated calcification, but no evidence of disease affecting the pulmonary parenchyma. The radiograph of the hip was interpreted as showing irregularity of the medial border of the neck of the left femur and "generalized rarefaction".

Factors which clouded diagnosis in the case of this boy were the deplorable condition of his teeth and gums, and a vague statement of a familial tendency to excessive bleeding, but the possibilities of infective arthritis related to the septic state of his mouth and spontaneous hæmophilic hæmarthrosis were disposed of by the recovery of *Mycobacterium tuberculosis* from the gastric content. The utility and reliability of the bacteriological finding were amply confirmed by the subsequent course of events. Six years later the boy was still under observation and treatment, tuberculous disease in the left hip joint having progressed to cold abscess formation with all its implications. During this period he exhibited phlyctenular conjunctivitis and repeated attacks of hæmaturia. *Mycobacterium tuberculosis* was cultivated from the urine and renal tuberculosis eventually shown to be bilateral.

In the case of the second patient, a boy, aged two years, number 63 in the series, cultivation of *Mycobacterium tuberculosis* from the gastric content established the diagnosis of

tuberculosis of the hip joint in a phase in which the only point in clinical evidence was the child's reactivity to the Mantoux intradermal test; radiographic signs were altogether lacking in the hip joint and inconclusive in the thorax. When brought to the Children's Hospital on February 27, 1945, the child was said to have been limping for three weeks. No family history of tuberculosis could be elicited. Two radiographs, of February 27 and March 7 respectively, failed to show any changes affecting the bones of the hip joint, and the report on a thoracic radiograph, taken on the later of these two dates, noted nothing more committal than exaggerated bronchial markings in the hilar region of the right lung. Nevertheless *Mycobacterium tuberculosis* appeared in culture tubes inoculated with deposit from appropriately treated gastric content, withdrawn four days after the child's admission to hospital. He was transferred to the Orthopædic Section of the Children's Hospital, Frankston, where subsequent events substantiated the diagnosis of tuberculosis of the hip joint, and where he died of meningeal tuberculosis in November, 1946.

It is to be expected that in a proportion of children on whose behalf treatment is sought for a disability which eventuates as one or other manifestation of skeletal tuberculosis, the primary complex to which the bone or joint tuberculosis stands in metastatic relation will be so far from quiescent as regards its pulmonary component as to render possible the interception of tubercle bacilli eliminated therefrom by an appropriate method of cultivation applied to the gastric content. In several of the 15 children grouped as subjects of skeletal tuberculosis by reason of their presenting and subsequently dominating clinical aspects, *Mycobacterium tuberculosis* was recovered from the gastric content at intervals during a period of many months, and in the case of a little girl, aged four years, number 61 in the series, this secretion was still a source from which tubercle bacilli might be cultivated two and a half years after a limp of two weeks' duration had brought her under observation for the first time on January 24, 1945. Her long succession of positive bacteriological findings was initiated by the recovery of *Mycobacterium tuberculosis* from three consecutive samples of gastric content withdrawn within a week of her first appearance. The child sustained tuberculous disease of both hip joints and ultimately, after the lapse of four years, achieved ankylosis. The demonstration of persistently active tuberculous pulmonary lesions, as was effected to a notable degree in the children numbered 41 and 61 in this series, in both of whom involvement of two joints was the clinical expression of tuberculous disease, indicates the necessity for close attention to the medical aspects of so-called "surgical" tuberculosis.

In two of the children in whom the presenting manifestation of tuberculosis was a morbid process involving bone, the site of disease was the mastoid process of the temporal bone.

The first of these, number 29, an infant, aged eleven weeks, was brought to hospital for the treatment of left-sided otorrhœa, which was said to have been of two weeks' duration. The baby's mother being known to be a subject of active pulmonary tuberculosis, a Ziehl-Neelsen preparation was included in the bacteriological procedures applied to the discharge from the child's ear. Acid-fast bacilli were detected by direct microscopic search of the aural discharge, as they were by similar means in a smear preparation of the deposit from the gastric mucus as prepared for cultivation. The cultural characteristics of the acid-fast bacilli confirmed them as representatives of the human type of *Mycobacterium tuberculosis*. The presence of tubercle bacilli in numbers sufficient to render them readily detectable by the search of smear preparations of both the aural discharge and the gastric mucus suggested very strongly that in this instance tubercle bacilli reached the stomach by traversing the natural passages of the Eustachian tube, pharynx and œsophagus, and that the otitic lesion contributed more to the positive bacteriological findings yielded by the gastric content than the usual source of such determinations, namely, a tuberculous process in the parenchyma of the lung. This impression was confirmed at autopsy following the baby's death at the age of seventeen weeks, the examination revealing miliary tuberculosis *sine* meningitis, a pulmonary complex in which the parenchymal constituent was so small as almost to elude detection, extensive tuberculous ulceration of the ileal mucous membrane, heavy involvement of the mesenteric lymph nodes, and bilateral tuberculous otitis and mastoiditis. The tuberculous ulcers in the mucous membrane of the lower reaches of the small intestine were no doubt to be referred to the activities of bacilli conveyed to the bowel in the heavily charged gastric content, and the sum of the autopsy findings indicated the source of such bacilli as the bilateral otitis and mastoiditis rather than the lung.

The second patient to exhibit tuberculous mastoiditis, a male infant, aged nine months, who provided number 66 in the series of cultures of *Mycobacterium tuberculosis* recovered from gastric content, came to the Children's Hospital on June 6, 1945, with the diagnosis of tuberculous otorrhœa established by Dr. Andrew Brenan's report on a biopsy specimen of granulation tissue taken during a period in which the baby was under supervision in a private hospital. A thoracic radiograph of June 23 was read as showing consolidation in the upper lobe of the left lung, and mottling dispersed through both lungs. The baby made no progress in his three months' stay at the Children's Hospital and was taken home at the end of this period.

In considering the pathogenesis of tuberculous otitis and mastoiditis, hæmatogenous infection can never be excluded in such an essentially metastasizing disease, but it would seem at least equally probable that the lesions in question may be placed in the category of infection due to the conveyance of bacilli along natural channels. Implantation of tubercle bacilli on the naso-pharyngeal mucous membrane may follow inhalation of the micro-organisms, as witness the fact that they have often been detected in adenoid vegetations. Bacilli which reach the gastric content do so only by traversing the pharynx, to which point in transit they are delivered by coughing or by the action of the cilia of the tracheo-bronchial epithelium. In the latter event the act of "clearing the throat" and swallowing completes the process of transfer from the respiratory to the alimentary system. Transportation of bacilli from the pharynx by ever-ready macrophages might well result in their lodgement and resumption of activity in the middle ear.

As a help in time of diagnostic trouble cultivation of *Mycobacterium tuberculosis* from the gastric mucus proved to the particular advantage of three children, represented by the numbers 32, 63 and 67, for none of whom was any assistance in the elucidation of his individual problem forthcoming by X-ray examination of the affected joint. In the order named these children sought treatment for disability affecting the tarsus, hip joint, and knee joint respectively.

"Radiographic Lag" in Skeletal Tuberculosis.

It is not to be expected that a single X-ray examination made early in the course of tuberculous disease of a bone or joint will always reveal a process destined to progress and effect demonstrable changes at a later date. What Brailsford (1946) has termed the "radiographic lag"—the period required for a lesion to attain macroscopic dimensions and effect the modifications in tissue density necessary to render it detectable radiographically—must operate in skeletal as in pulmonary tuberculosis. The positive findings with respect to tuberculosis attending bacteriological investigation of the content of the fasting stomachs of the three children mentioned illustrate the utility of this procedure applied in the interval of "radiographic lag".

It is particularly when tuberculous infection is initiated in the synovial membrane that it may elude radiographic recognition for a period which the frequently slow progress of tuberculous arthritis may determine as prolonged. It has always been a moot point, and one difficult of elucidation in any individual instance, whether tuberculous arthritis commences in the epiphysis of one of the bones participating in the articulation or in the synovial membrane. Both modes of origin undoubtedly operate, and in either event the infection is hæmatogenous and an expression of the predisposition of tubercle bacilli to lodge in regions well endowed with respect to vascular spaces and ramifying vessels. In all probability the first step in the genesis of tuberculous arthritis is the induction of tuberculous endarteritis either in the cancellous bone of the epiphysis or in the vessels of the *circulus vascularis*, which marks the reflection of synovial membrane onto bone. In the latter contingency a tuberculous synovitis ensues and the disease process subsequently spreads from the synovia to the adjacent bone.

Interesting considerations regarding the probability that tuberculosis of joints is more often than not initiated in the synovial membrane have been advanced by C. A. Ryan (1949). He regards as significant the clinical fact that the earliest symptoms of tuberculosis of bone are referred to the joint to a predominating extent, and interprets this observation as indicating that the synovia is primarily involved. He finds support for this view in an examination of the types of tuberculous lesions which occur in the upper and lower ends of the femur respectively, pointing out that at the upper end of the femur the synovial membrane is reflected well down on the metaphysis, with the result that metaphyseal tuberculosis is frequently seen at the proximal end of the femur. At the lower or distal end of the femur, *per contra*, the reflection of the synovial membrane is contained within the limits of the epiphysis, and epiphyseal rather than metaphyseal tuberculosis is found in this situation. The author named suggests that if the precise pathological process could be determined at a sufficiently early stage of the arthropathy it would be found that all tuberculosis of joints commences as tuberculous synovitis.

Renal Tuberculosis.

Skeletal tuberculosis exposes patients so affected to an enhanced risk of renal tuberculosis, and two of the 15 children in whom the recovery of *Mycobacterium tuberculosis* from the gastric mucus established the diagnosis of osseous tuberculosis in an early phase of its course fell at this hazard. The clinical features of one boy, number 17, have already been outlined; the other was a boy, aged seven and a half years, number 81, whose left kidney was removed after he had endured the protracted illness inseparable from tuberculosis of the spine for five and a half years. The operation of nephrectomy was clearly indicated by persistent pyuria, repeated cultivations of *Mycobacterium tuberculosis* from the bladder urine, and the ultimate recovery of this microorganism from urine withdrawn from the pelvis of the left kidney by ureteral catheterization.

In an earlier communication (1941) I have published my findings in a study directed towards ascertaining the frequency with which tuberculous bacilluria may be demonstrated in persons whose dominant clinical manifestations are skeletal and pulmonary disease respectively. The bacteriological examinations of the urine were undertaken irrespective of the presence of signs or symptoms indicating implication of th urinary system. Of 18 children, inmates of the Orthopædic Section of the Children's Hospital by reason of skeletal tuberculosis, six were shown to be eliminating tubercle bacilli in the urine, and of 64 adult patients of the Austin Hospital, suffering from tuberculosis of the spine, hip, or other joint, no less than 32 (50%) exhibited tuberculous bacilluria. A similar survey of specimens of urine from 117 adults, patients of the Austin Hospital and Gresswell Sanatorium, and all suffering from pulmonary tuberculosis in an active phase, determined that 30 (25·6%) were discharging tubercle bacilli in the urine. Based as they were, in the main, on a single bacteriological examination of the urine of individual patients, the results obtained almost certainly under-estimated the incidence of tuberculous bacilluria in the subjects of skeletal and pulmonary tuberculosis. Many, indeed the majority of persons investigated, were free of symptoms such as would draw attention to the urinary system; some indeed exhibited no signs detectable by microscopic examination of the urinary deposit, but it has been shown (Medlar and Sasano, 1924-1925; Medlar, 1926; Band, 1935) that the presence of tubercle bacilli in the urine implies tuberculous infection of the kidneys as a necessity, and that the conception of "excretory bacilluria" is untenable. The lesions induced are often of microscopic dimensions, possibly no more than minute interstitial foci which make communication with adjoining tubules, or erosions involving glomeruli; they may excite no symptoms and lie beyond the range of clinical perception. Fortunately many such minimal lesions heal, and only a minority progress to the destruction and cavitation—renal phthisis—which demand nephrectomy.

Clinically manifest tuberculosis has been well said to be a disease characterized by repeated episodes of metastasis and body reaction. In a disorder so essentially systemic any active tuberculous focus may be the source of renal metastatic lesions, but the particular susceptibility to renal tuberculosis of subjects of osseous disease is referable to the fact that, by the metastatic induction of bone and joint tuberculosis, the invading bacilli succeed in establishing a forward base in a site particularly favourable for their further access to the circulation.

Human and Bovine Tubercle Bacilli in Bone and Joint Tuberculosis.

The cultures of *Mycobacterium tuberculosis* recovered from the gastric mucus of every one of the 162 children who provided the basis for this report were of eugonic, glycerophilic and distinctly human type, and included among them were 15 children whose conspicuous clinical disease was tuberculosis of bones and joints. Concerning the possible operation of the bovine type of *Mycobacterium tuberculosis* in childhood, I have nothing to add to what I have already written (1941), except to repeat that the notion that the bovine bacillus plays a large part in tuberculosis of bones and joints in this country seems as tenacious as it is undoubtedly fallacious. In 96 cultures of *Mycobacterium tuberculosis* of which I have records as differentiated with respect to type, and obtained from pathological exudates or granulation tissue derived directly from tuberculous lesions of bone, the bovine type is not even represented. The impression that the bovine tubercle bacillus figures largely in "surgical" tuberculosis has no doubt been gained from text-books emanating from Great Britain, in which country the bovine bacillus has been implicated in skeletal tuberculosis to a much greater extent than in Australia or the United States of America.

References.

Band, David (1935), "Renal Tuberculosis", *Edinburgh Medical Journal*, Volume XLII, page 162.

Brailsford, J. S. (1946), "Evaluation of the Negative Radiological Report", *The Practitioner*, Volume CLVII, page 200.

Medlar, E. M. (1926), "Cases of Renal Infection in Pulmonary Tuberculosis: Evidence of Healed Lesions", *The American Journal of Pathology* (September), page 421.

——— and Kasano, K. T. (1924-1925), "Experimental Renal Tuberculosis. With Special Reference to Excretory Bacilluria", *The American Review of Tuberculosis*, Volume X, page 370.

Ryan, C. A. (1949), "Tuberculosis of Bones and Joints", *The Journal of the International College of Surgeons*, Volume XII, page 36.

Webster, R. (1941), "Symptomless Tuberculous Bacilluria: As Observed in Subjects of Osseous and Pulmonary Tuberculosis", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 217.

——— (1941), "The Relative Incidence of Human and Bovine Types of Mycobacterium Tuberculosis in Human Disease in Victoria", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 49.

TUBERCULOSIS OF THE CERVICAL LYMPH NODES.

Enlargement of the cervical lymph nodes was a prominent clinical feature in five of the children from whose gastric mucus *Mycobacterium tuberculosis* was cultivated. That the lymph-nodal swelling represented an intercurrent non-tuberculous infection in the course of primary tuberculous infection of the lung is a legitimate inference with respect to the two children who provided gastric content cultures number 42 and number 123. The former derived from a little girl whose evanescent lymph-nodal swellings subsided three days after her admission to hospital, and the latter from a boy in whom the inflammatory process in the cervical lymph nodes progressed to suppuration; *Staphylococcus aureus* was cultivated from the evacuated pus and all efforts to demonstrate the presence of tubercle bacilli failed.

The remaining three children present the problem of the pathogenesis of tuberculosis of the cervical lymph nodes in the presence of a tuberculous pulmonary lesion, the existence of which was established by radiographic signs and the cultivation of tubercle bacilli from the gastric content. In general it may be stated that the cervical lymph nodes may become involved in tuberculosis as

participants in a primary complex, the initial tuberculous focus of which is located in the tonsil, pharyngeal adenoid vegetations, middle ear, or even on the face; access of tubercle bacilli to lymph nodes in the neck may also be effected by their steady progression from the hilar lymph node component of a pulmonary primary complex to the paratracheal nodes, and thence to the inferior cervical nodes; further, the notorious affinity of tubercle bacilli for lymphoid tissue renders the cervical, in common with other lymph nodes, vulnerable to bacilli dispersed in the recurring episodes of silent bacteriæmia which are inseparable from tuberculous infection sufficiently active to be clinically manifest.

The determination of the precise sequence of events in each of the three children under consideration is rendered difficult by deficiencies in the information relating to them, but with respect to the child from whose gastric mucus the culture of *Mycobacterium tuberculosis* number 13 was recovered, the available data suggest strongly that the tuberculous infection of the cervical lymph nodes was hæmatogenous and of metastatic nature.

The patient, a boy, aged five years, was admitted to the Children's Hospital as having been drowsy, listless, and feverish for approximately ten weeks. He reacted to the Mantoux intradermal tuberculin test, and the notes relating to the family history record his father as a subject of pulmonary tuberculosis, "apparently cured". The lymph nodes on both sides of the neck were observed to be enlarged, but no precise date could be affixed by the parents to the appearance of this clinical feature. A thoracic radiograph revealed consolidation of the inferior portion of the upper lobe of the right lung, conspicuous exaggeration of the hilar shadow, and diffuse mottling throughout both lungs. One month later the dispersed lesions in the lungs, presumably bronchopneumonic, were observed radiographically to have progressed. In the meantime, acid-fast bacilli had been demonstrated by microscopic search of a smear preparation of deposit from the child's gastric content, and their identity as *Mycobacterium tuberculosis* confirmed by cultivation. During his five weeks' stay in the Children's Hospital the boy displayed a "swinging" temperature, distended abdomen, and progressive loss of weight; a very sick child, he was taken home on August 20, 1940, the clinical estimate of his condition being one of pulmonary and glandular tuberculosis and tuberculous peritonitis.

That tuberculosis of the cervical lymph nodes was contributory to a primary complex would seem to be the conclusion indicated by the clinical facts relating to a little girl, aged five years and three months, from whose gastric content number 33 in the series of cultures of *Mycobacterium tuberculosis* from this source was obtained. Pulmonary tuberculosis in her mother declared itself shortly after the baby's birth. When the infant was fifteen months old enlarged and caseating lymph nodes of the upper cervical group on the right side were excised at the Alfred Hospital and subsequently proved tuberculous bacteriologically. Four years later the child presented at the Children's Hospital, exhibiting a small cluster of enlarged lymph nodes in the immediate vicinity of an operative scar in the carotid triangle of the right side of the neck. The report on a thoracic radiograph noted an unduly large hilar shadow and prominent pulmonary markings in the lower lobe of the right lung, adding that there was no radiographic suggestion of active infiltration. The cultivation of *Mycobacterium tuberculosis* from a sample of gastric content withdrawn at this time provided yet another instance of the presence of living tubercle bacilli in lesions which by radiographic standards would be considered "inactive" or "closed". No untoward incident attended the excision of the second small group of tuberculous cervical lymph nodes.

It would seem most probable that in this particular child the bacilli causing primary infection gained access by two portals and established disease foci in the lung and in the pharynx, with lymph nodal complements located in the hilar and cervical lymph nodes respectively. Important considerations are that the child's mother was a subject of pulmonary tuberculosis and that the tubercle bacilli recovered from the little girl's gastric content were of human type. The possibility that the tuberculous infection of the cervical lymph nodes was referable to the ingestion of milk conveying bovine tubercle bacilli, as has been so frequently the case in the past, hinges on the remote contingency of infection by both human and bovine types of tubercle bacilli, the former installing themselves in the lung and the latter in the cervical lymph nodes. Of double infection of this nature I have met with only one instance, duly reported (1941), among 387 patients, children and adults, the cultures of *Mycobacterium tuberculosis* recovered from whom have been differentiated with respect to human or bovine type. A. Stanley Griffith, the doyen of the school in all matters relating to relative incidence of infection by human and bovine types of *Mycobacterium tuberculosis*, has recorded (1937) "mixed"—I prefer the term "double"—infection as having occurred only 11 times in more than 6000 examinations in Great Britain, K. A. Jensen (1937) six times in 3000 examinations in Denmark, and Bruno Lange (1932) eight times in 1027 examinations made in Germany up to the year 1932.

Tubercle bacilli are most commonly conveyed by inhalation to the lung, but there is nothing inherently improbable in the idea that some among the inhaled microorganisms may fall by the wayside, and, detained on adenoid vegetations or in tonsillar crypts, be subsequently diverted to the cervical lymph nodes. Further, no exception may be taken to the suggestion of the induction of more than one primary complex, the possibility of which has been discussed in an earlier section of this commentary.

The likelihood of the pulmonary infection having been determined by endogenous reinfection based on the tuberculous process in the cervical lymph nodes is heavily discounted by the consideration that radiographic evidence indicated the site of the pulmonary involvement as the lower lobe of the right lung, and to accede to the view of endogenous reinfection would involve a violation of the cardinal principle that the lesion of reinfection exhibits a constant predilection for the upper lobes of the lungs. No such limitation applies to the location of primary foci, which may be situated anywhere in the peripheral pulmonary tissue.

Could tubercle bacilli have reached the cervical lymph nodes in this instance by a steady march from a pulmonary focus and the initially implicated broncho-pulmonary lymph nodes to the hilar and paratracheal nodes, and thence to the cervical nodes? Such a progression has been observed in morbid anatomical studies and the curious fact has been demonstrated that while lymphatic communications exist between the hilar lymph nodes and the cervical, no lymph flow passes in the opposite direction. Should the disease in the cervical lymph nodes have reached them indirectly by lymphatic spread of infection from a pulmonary complex in the child under discussion, it must have become evident first in the inferior cervical lymph nodes, whereas both initially and in its recurrence it was located in the lymph nodes in the vicinity of the carotid triangle. Hence, as far as the recorded facts permit a conclusion, this child is presented as exemplifying the occurrence of coexisting pulmonary and pharyngeal primary complexes.

The third child (number 79) to present with tuberculosis of the cervical lymph nodes and subsequently yield cultures of *Mycobacterium tuberculosis* from the gastric content first appeared in the out-patient department on December 13, 1944, at the age of eleven months. The infant displayed a chain of enlarged lymph nodes extending from the occiput to the clavicle on the left side of the neck. She reacted unequivocally to the Mantoux intradermal test performed with 0·1 millilitre of a 1 in 1000 dilution of old tuberculin. No evidence of domiciliary contact could be determined. On February 7, 1945, eight weeks after the baby's first attendance, softening was observed in the affected lymph nodes and aspiration yielded caseous material in which tubercle bacilli were readily demonstrable. The clinical record lacks information regarding radiography of the chest prior to April 4, 1946, approximately sixteen months after the child came under observation for the first time. The report on a radiograph taken on the date named, and while the child was still attending an out-patient clinic, recorded the presence of a calcified primary focus in the upper zone of the right lung and infiltration of doubtful ætiology in the apical region of the lung. Two months later, June 11, 1946, the child, then aged two years and five months, was admitted to hospital on account of general indisposition, the leading features of which were loss of weight, vomiting, and epistaxes. The report on a radiograph of the chest taken on the day following the child's admission confirmed the earlier finding of infiltration in the apical region of the right lung, remarked that the shadow showed incipient stippling, and noted the presence of hazy opacity in the middle lobe of the right lung. No mention was made of a

calcified primary lesion. At this stage *Mycobacterium tuberculosis* was cultivated from the patient's gastric content.

Tuberculosis of the cervical lymph nodes was the presenting, and for a time the dominant, feature in the illness of this child, but determination of its status in pathogenesis is rendered difficult by the fact that an interval of sixteen months elapsed between the recognition of a tuberculous process affecting the cervical lymph nodes and the first recorded radiographic examination of the chest, and by the failure of the radiological reports to agree on the critical point of the presence of a calcified primary focus. The existence of such a focus, noted as present in the radiologist's report of April 4, 1946, but not recorded in that of June 12, would have created a situation parallel with that examined in the case of the immediately preceding child (number 33), and suggested the entry of the infecting bacilli by two portals to initiate pharyngeal and pulmonary primary complexes. On the other hand, the radiologist's report of June 12, 1946, would conform well with an interpretation of the pulmonary lesion as a manifestation of reinfection deriving from the cervical lymph nodes. And there, perforce, the question must rest.

The Pharyngeal Primary Complex.

Of the three possible modes of involvement of the cervical lymph nodes in tuberculous infection, I am convinced that the most frequent is that of primary infection, the lymph nodes of the neck contributing to a primary complex, of which the lesion of entry is located in the pharynx, and most commonly in the tonsil of the affected side. The prominence assumed by the lymph nodal component of such a complex is a consistent feature of the morbid changes induced by primary infection wherever it may be established, be it in the lung, pharynx, intestine, conjunctiva or the skin. The pathogenesis of tuberculosis of the cervical lymph nodes presents no problem in those instances in which the bovine type of *Mycobacterium tuberculosis* is implicated, such determinations clearly indicating infection by the ingestion of tuberculous milk and detention of tubercle bacilli in tonsillar crypts or in the recesses of adenoid vegetations. A high incidence of bovine infection in tuberculosis of the cervical lymph nodes has been found by all workers who have studied the question, and my own finding (1941) of 31 bovine strains among 54 cultures of *Mycobacterium tuberculosis* recovered from cervical lymph nodes and/or tonsils is in agreement with results obtained by workers in other countries. Tubercle bacilli of human type conveyed on inspired air may with equal facility lodge at one or other point in the pharyngeal lymphoid tissue disposed in the eponymously styled ring of Waldeyer and initiate primary infection with its inevitable involvement of the regional lymph nodes.

My own observations (1932) on the site of a pharyngeal lesion of entry of tubercle bacilli which eventually induce tuberculous changes in the cervical lymph nodes are confined to the tonsils and do not embrace adenoid vegetations. In one or other tonsil, or both, of 70 children suffering from tuberculosis of the cervical lymph nodes I found evidence of tuberculosis in 31 instances by histological study alone; in 16 other children similarly affected the examination of microscopic sections was supplemented by animal inoculation, with the result that a positive finding with respect to tuberculosis of the tonsil was recorded in nine of the 16 patients. In all, the tonsils of 86 children, all under the age of fourteen years and subjects of tuberculous glands of the neck, were examined; tuberculosis of one or both tonsils was established in 40, or 46·5% of the number of children covered by the investigation. In those instances in which tuberculous infection was demonstrable in one tonsil only, it was invariably on the same side as the tuberculous lymph nodes. The figure obtained was undoubtedly an under-estimate, the histological examination being admittedly not exhaustive. The relentless pressure of work relating to both the quick and the dead in a hospital department of routine pathology did not permit of serial sections, and the number prepared and examined in any individual instance was determined by the urgency of requirements in other directions.

While I would be the last to discount the necessity for accurate bacteriological diagnosis, and consider that the objective of laboratory procedures directed towards the identification of tuberculous processes should be the demonstration of the presence of *Mycobacterium tuberculosis* whenever possible, I would at the same time maintain that histological evidence of tuberculosis of the tonsil, when it is found, is thoroughly convincing and satisfactory. All stages in the formation of the typical "tubercle follicle" are to be seen, and caseation on a limited scale is to be observed; almost invariably the surface epithelium of the tonsil is intact. The tubercle follicles are often seen in the immediate neighbourhood of a tonsillar crypt, and in tonsils badly infected, discrete and confluent follicles may be seen throughout the section.

It is in the demonstration of tissue reaction that the histological method has perhaps a point of advantage over the detection of *Mycobacterium tuberculosis* by cultivation or animal inoculation. The specific tissue reaction of necessity implies invasion of the tonsil and pathogenic activity on the part of the tubercle bacillus, whereas the recovery of the microorganism by cultivation from tonsillar tissue or the induction of tuberculosis in a guinea-pig by the injection of tonsillar pulp demonstrates nothing more than the presence of tubercle bacilli. Such bacilli might have been haunting tonsillar crypts without ever having effected a tuberculous lesion. The ideal, of course, is to carry out both methods of investigation, but I am of opinion that when histological evidence alone is available, it is quite reliable. The inoculation test is not without its fallacies, the discussion of which would prolong what is already, I fear, a digression.

On many occasions since the publication of the above quoted findings have I detected tuberculous infection in a tonsil of the same side as tuberculous cervical lymph nodes, but neither in the original series nor at any time since have I encountered a single instance in which there was any macroscopic indication of the tuberculous process subsequently revealed. This striking and somewhat perplexing feature of the lesion of entry in a pharyngeal primary complex renders it improbable that the tubercle bacilli cultivated from the gastric mucus of the three children around whom this discussion has been woven were eliminated from the tonsil and conveyed to the stomach in swallowed saliva. Supported by radiological findings, I have treated the tubercle bacilli cultivated from the gastric mucus as having emanated from a pulmonary lesion, and considered the three children as having exhibited coexisting pulmonary and cervical lymph node tuberculosis. In the patients represented by the numbers 33 and 79, tuberculosis of the cervical lymph nodes was the presenting and dominant clinical feature.

References.

Griffith, A. Stanley (1937), "Mixed Infections with Human and Bovine Tubercle Bacilli in the Human Subject", *Tubercle*, Volume XVIII, page 193.

Jensen, K. A. (1937), cited by A. Stanley Griffith, *loco citato*.

Lange, Bruno (1932), "The Role Played by Bovine Tubercle Bacilli in Human Tuberculosis", *British Medical Journal*, Volume II, page 503.

Webster, R. (1932), "Occult Tuberculosis of the Tonsil in Relation to Tuberculous Cervical Adenitis", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 351.

——— (1941), "The Relative Incidence of Human and Bovine Types of Mycobacterium Tuberculosis in Human Disease in Victoria", *ibidem*, Volume II, page 49.

SUMMARY.

1. An endeavour has been made to assess precisely the morbid changes from which derived 162 cultures of *Mycobacterium tuberculosis* recovered from the gastric content of as many individual children, and to elucidate incidental problems in pathogenesis and immunology.

2. Despite unequivocal bacteriological diagnosis of tuberculosis, eight of the 162 children were found insensitive to tuberculin; comment upon this fact involved brief consideration of conditions inducing fluctuations in tuberculin sensitivity.

3. Of the 162 children 90 were exposed to the hazard of household contact with relatives in high degree infective; contact rather less intimate than familial was recorded for 25 children, 37 were conceded a clean sheet in this respect, and for 10 information on the point was lacking. The repeated inoculations by inhalation implicit in household contact are considered in relation to the fact that primary pulmonary lesions in children are much more frequently single than multiple, and it is suggested that the apparent paradox is explicable by the application of the theory of infection-immunity. The possibility that a succession of inoculating doses may act as a stimulus to resistance, and operate to determine a more favourable course in tuberculosis thus acquired than in that ensuing on infection by casual contact, is also explored.

4. *Mycobacterium tuberculosis* was recovered from the gastric content of 18 children who presented with one or other expression of the hypersensitive state, namely: "tuberculous rheumatism" (5), *erythema nodosum* (8), phlyctenular conjunctivitis (5). The immunological mechanism underlying such manifestations of tuberculous infection is examined.

5. In 26 instances a gastric mucous culture of *Mycobacterium tuberculosis* was adduced in corroboration of the diagnosis of meningeal tuberculosis. In the series there were eight examples of the independent occurrence of the frequently associated states, miliary tuberculosis and tuberculous meningitis. In four children the finding *post mortem* was one of meningeal tuberculosis *sine* miliary tuberculosis; in the other four an extreme degree of miliary tuberculosis was unaccompanied by tuberculous meningitis, but in three of the four autopsy disclosed the presence of significant juxta-meningeal caseous foci. The observations in these three children are detailed as supporting the contention that meningeal tuberculosis is to be referred to extension of infection from an intracranial "parent focus" rather than to immediate hæmatogenous infection. Emphasis is laid on the importance of the vascular lesions in tuberculous meningitis, and a case record cited as evidence of the possibility that meningeal tuberculosis may precede and precipitate miliary tuberculosis.

6. Pulmonary manifestations of tuberculous infection predominated in 90 of the children, the clinical aspect of 17 suggesting pneumonia of acute onset; vague ill-health, often dating from antecedent measles, brought 49 other children under observation, while the pulmonary tuberculous process in the remaining 24 was detected by routine examination of familial contacts.

7. Tuberculous pneumonia of acute onset and lobar dimensions is described, and lengthy consideration given to the occurrence of pulmonary collapse, to which the question of epituberculosis is related. In 24 of 90 children in whom the clinical or radiological expression of tuberculosis was pulmonary disease, the morbid process in the lung from which the gastric content culture of *Mycobacterium tuberculosis* was derived was dominated by collapse.

8. Bronchial occlusion, with its sequelæ lobar or segmental collapse and ensuing bronchiectasis, was demonstrated in all the recorded instances by Howard Williams, to whose concurrent bronchoscopic studies much of the bacteriological work on which this communication is based was complementary.

9. Of particular interest were the 24 apparently healthy children examined as familial "contacts", in whom tubercle bacilli emanated from disease processes which were in some instances beyond the range of radiological perception, and in others were revealed radiographically as incredibly extensive, even embracing miliary tuberculosis. Six of the "healthy" contact children were found by Howard Williams to exhibit varying degrees of pulmonary collapse and residual bronchiectasis.

10. In three instances the bacteriological finding indicated pulmonary tuberculosis as provocative of an initial hæmoptysis, an uncommon event in childhood.

11. The presumed tuberculous basis of "primary" pleurisy with effusion was confirmed by the recovery of *Mycobacterium tuberculosis* from the gastric reservoir in ten cases. Brief comment on the case records of three children in the group is followed by discussion of the pathogenesis of tuberculous pleurisy.

12. A positive bacteriological finding yielded by the gastric mucus established or confirmed the diagnosis of skeletal tuberculosis in 15 children. Notes of the clinical features of selected patients are followed by comments which emphasize (*a*) the tendency to "radiographic lag", (*b*) the liability to renal tuberculosis, and (*c*) the invariable operation—in Australia—of the human type of *Mycobacterium tuberculosis* in tuberculosis of bones and joints.

13. Five children whose gastric content was a source of tubercle bacilli presented with enlargement of the cervical lymph nodes. The probable paths by which tubercle bacilli reached the cervical lymph nodes in three children of the group are suggested. The view is advanced that tuberculous cervical lymph nodes occur most frequently as participants in a pharyngeal primary complex. Bacteriological findings are adduced as substantiating the statement that in Australia the bovine type of *Mycobacterium tuberculosis* finds its principal field of activity in the human subject in the tonsils and cervical glands.

14. Correlation of radiological and bacteriological findings revealed not infrequent discrepancies, one conspicuous example of which led to examination of the question of tubercle bacillus "carriers".

ACKNOWLEDGEMENTS.

I wish to acknowledge gratefully the assistance I have received from my technician and associate of many years, the late Mr. H. Weir, upon whom devolved the preparation of large quantities of culture medium, and much clerical and laboratory bench work. Since deteriorating health enforced Mr. Weir's retirement in August, 1951, his place has been capably taken by Mr. L. A. Foulger. To the members of the honorary staff of the Children's Hospital, and the efficient courtesy of the clerical staffs of the in-patient and out-patient records offices, I am indebted for access to clinical histories, and for the photographs to the photographic unit of the hospital, directed by Mr. C. Murphy. Figures II and IV are reproduced by courtesy of the Melbourne University Press.

Reviews.

THE AUSTRALIAN MEDICAL HISTORY OF THE WAR.

THE first volume of what will eventually become known as the "Australian Medical History of the War" has been published under the title "Clinical Problems of the War".[1] The volume is the work of Dr. Allan S. Walker and it has been published by the Australian War Memorial at Canberra. In June, 1945, Dr. Walker's appointment as medical war historian in succession to the late Major-General R. M. Downes was announced in this journal and the wisdom of the appointment was commented upon; this first volume shows that the widely held belief of his suitability for the work has been fully justified. The part played by Australia in the war of 1939-1945 will be described in five series of volumes. Series I (Army) will consist of seven volumes; Series II (Navy) will comprise two volumes; Series III (Air) will contain four volumes; Series IV (Civil) five volumes; all these will be the work of several authors. Series V (Medical) contains four volumes. The General Editor of the War History is Mr. Gavin Long. The four volumes of the medical group will be: (*a*) "Clinical Problems of the War", the volume under review; (*b*) "Middle East and Far East"; (*c*) "The Island Campaigns"; (*d*) "Medical Services of R.A.N. and R.A.A.F."; all will be the work of Dr. Walker. In his preface to the present volume Dr. Walker states that clinical volumes were included in the

[1] "The Official History of Australia in the War of 1939-1945; Series V (Medical); Volume I: Clinical Problems of the War", by Allan S. Walker, M.D., F.R.A.C.P.; 1952. Canberra: Australian War Memorial. Sydney: Angus and Robertson, Limited. 9½" × 6¼", pp. 712, with 15 maps and diagrams and 73 photographs. Price: 35s.

plan originally drawn up by the late R. M. Downes, who intended that they should consist of articles written by medical officers. But even in the short time at his disposal Downes experienced difficulties and Dr. Walker later on experienced them too. "Such accounts could only be properly written with access to relevant records, and preferably during the officers' military service, but this was not practicable." The result was that the actual writing of the clinical volume became, with the exception of a few sections, a single-handed task. Few men could have done this, and the way in which Dr. Walker has done it will stand to his lasting credit. He had the advantage of serving for a period as one of the consulting physicians of the Australian Imperial Force; in this capacity he had access to many sources of information and he had a hand in or saw many of the developments and advances which he describes. It is necessary to explain the scope of the book. The author states that it is neither a text-book nor a military manual. It deals with administration only where this is germane to the control of disease or injury. There is no pretence to cover the whole of any subject; on the other hand the book records Australian experience, the methods found valuable, the successes and the failures. At the same time it is complementary to the other volumes of the medical series, which are being prepared—it will not "rob" these volumes, but it "is designed to show how the doctor remains the doctor even in an environment largely foreign to him".

The introduction to this volume is a prologue in which attention is drawn to the changes in medicine in the first half of this century and particularly in the period between the two World Wars—the scientific method came into prominence and specialism arose and increased. In spite of all the changes and developments in every sphere of life, emphasis in health and disease remained on the individual—"in a world of failing individualism the medical profession stands out as one of the few social groups to champion the single soul". In civilian life those medical men and women whose overall knowledge of medicine is widest, whose capacity to serve the public is greatest, and who are of most value to the community in peace and war are the general practitioners. So in wartime it is the "individual plain doctor plying his uniformed calling in a manner consonant with his training and his instincts" who sets the background of the complex medical organization in the military sphere. In the author's opinion it is therefore logical that his medical history should begin with an account of the purely medical problems of doctors on service.

The book is divided into three parts; the first is medical, the second is surgical, and the third deals with "special subjects". The first part is subdivided into three sections headed respectively "Infectious Diseases", "Systematic and Constitutional Affections", and "Disturbances due to Nutritional and Physical Causes". There are in addition to the prologue 61 chapters, with an epilogue and an index. At the end of each chapter a list of references appears and it is pleasing to note that a large number of them are to this journal.

In the first chapter the story of bacillary dysentery is told. Control was achieved, but the disease always broke out again when preventive discipline slackened. The author thinks that possibly the relative mastery over the disease tended to obscure its military importance. The most important advances were the use of the appropriate sulphonamides and the routine use of sigmoidoscopy in diagnosis. When these measures are applied to the civil community most clinicians realize that use of the sulphonamides has to be carefully controlled—these drugs destroy many of the normal bacterial inhabitants of the intestine as well as those that are pathological. Amœbiasis was not of great importance in the Australian armed forces, but infections were important because of the diagnostic and therapeutic problems involved and the disability caused. In the chapter on malaria the view is expressed that the loss of quinine to Japan was a blessing in disguise; "Atebrin" saved the day, though now it has yielded place to "Paludrine" and other anti-malarials. The story of malarial research at Cairns is told again. The L.H.Q. Medical Research Unit was established by the Commander-in-Chief, General Blamey, on the advice of the D.G.M.S., Major-General Burston. The plan evolved, we are told, was a cooperative project, but its original conception was due chiefly to Professor H. K. Ward, Colonel E. V. Keogh and Lieutenant-Colonel I. M. Mackerras. Colonel (later Brigadier) N. H. Fairley began the organization and was chiefly responsible for its success. The research unit at Cairns, which had its own establishment, was commanded first by Lieutenant-Colonel R. R. Andrew and later by Lieutenant-Colonel C. R. B. Blackburn. The work was described in this journal by Fairley in 1946 (one of the references is incorrectly given). In his concluding remarks about malaria, the author writes:

> We are better equipped than before in the war against this most destructive of protozoal diseases, but we still have to reckon with the recalcitrance of that possessor of high intelligence, man, who seems bent on destroying himself. It cannot be said that the very high overall rate of actual infection in the servicemen and servicewomen exposed to malarial hazards is entirely creditable. In theory we know how to prevent their infection, and how to suppress and partly to cure the resultant latent disease; and we have almost enough knowledge to cure the overt disease entirely and invariably when it occurs. In practice we have not successfully done all these things.

In the chapter on typhus fever, murine typhus, mite-borne typhus and tick-borne typhus are discussed; details of research work are given and mention is made of the tragic death of Miss Dora Lush, of the Walter and Eliza Hall Institute of Medical Research, who contracted a fatal attack of scrub typhus in the course of her work. In the chapter on cerebro-spinal meningitis the special instructions issued by the Military Board are reproduced, and the first published account of mass dosage of carriers with sulphapyridine to stop an epidemic of cerebro-spinal meningitis is referred to. This account by J. F. Meehan and C. R. Merrilees was published in this journal. A chapter on pyrexia of unknown origin, "P.U.O.", is short but important. Graham Butler is quoted as stating that "P.U.O. is a tribute to reality". This diagnosis was sometimes used because patients were transferred from forward medical units before thorough clinical observations could be made and when opportunities and facilities for investigations were lacking; even in fully equipped hospitals the diagnostic problem could not always be solved. A list is given of diseases which at times caused perplexity among medical officers. They are grouped as: (*a*) short-term fevers, (*b*) mild types of other infections, (*c*) continued fevers. We read that "it should be clearly realized that pyrexia of undetermined origin is a regional problem, whose solution may best be effected by close clinical survey, appropriate laboratory investigations and the study of its epidemiological features. Even after the most careful examination there will be an obscure residuum". A chapter is given over to respiratory diseases in which "U.R.T.I." and primary atypical pneumonia are discussed and this is followed by one on tuberculosis. In the latter fitting reference is made to the work of Major Reginald Webster on the examination of the gastric contents of recruits for tubercle bacilli. The story of pulmonary tuberculosis in the forces has, we read, twofold interest—"It tells of a step along the road of prevention, and a further step towards control." An important contribution to the war effort was the elimination of 1% of recruits who had suspected pulmonary disease; "so, too, was the coordination of treatment for a time under one authority".

A section of the medical part of the book is devoted to systematic and constitutional affections; here cardio-vascular diseases, chronic rheumatic diseases, dyspepsia, diseases of the central nervous system and diseases of the urinary tract are considered. The most significant chapter deals with dyspepsia. The author states that review of the whole war shows that digestive disease was of great importance in all armed forces. The harsh experiences of men held prisoner by the Japanese illustrated how an occasional or remittent lesion like a peptic ulcer occurring under reasonable conditions became a dangerous, permanent and progressive incubus when living was reduced to its lowest terms. At the other end of the scale it was seen how peptic ulcer recurred "under the stimulus of conditions of service, less flexible than those of ordinary life, particularly to the sensitive and unadaptable types". Dyspepsias of psychological origin were the commonest and, as can well be imagined, under arduous service conditions, the most difficult to treat.

In a section devoted to disturbances due to nutritional and physical causes are chapters on malnutrition, environmental conditions and poisoning. To describe these adequately would call for much more space than can be allowed. It must suffice to state that the author closes his searching and vivid description by reminding his readers that nutrition is perhaps the most important single problem facing the world, and he adds that the earnest studies made "under conditions of stringent restriction" help to lay emphasis on that problem.

In the second or surgical part of the book there are twenty-two chapters; every aspect of the subject seems to be included. In the chapter on war wounds it is pointed out that in 1939 modern transport had revolutionized war, and

the treatment of war wounds needed revision rather because of the effects of mobile warfare on the steady working of medical units than because of scientific considerations. Trueta's work on immobilization is discussed and the term *débridement* is explained. The controversy on primary suture is mentioned. It will be remembered that one consulting surgeon defended the procedure, provided proper safeguards were used, but that Colonel W. A. Hailes, consulting surgeon to the Australian Imperial Force, proscribed its use in uncompromising and severe terms. There were some who did not agree with this attitude, but the author states that "Hailes could do no other than lay down a definite safe rule". Wound treatment in the Middle East is described in one section and wound treatment in the Pacific campaigns in another. Chemotherapy is given a separate chapter. The author insists that the introduction and refinement of chemical or biological methods of limiting the development of bacteria in wounds must not *per se* be regarded as a revolution. While it is true that penicillin has in some respects revolutionized certain forms of treatment, "It is more correct to say that it has permitted a closer approximation to certain surgical ideals, and has helped strict adherence to surgical principles to win greater rewards". After a short discussion on surgical shock, there is a first-rate chapter on blood transfusion. This is based on a special contribution by Colonel I. J. Wood, with a special section on preparation, preservation and use of wet serum by Major R. J. Walsh. In the chapter on wounds of the lower extremity it is pointed out that in the Middle East the lot of men with fracture of the femur, even at its worst, was much better than in the early years of the 1914-1918 war—the Thomas splint did not have to fight for recognition. At the end of this chapter, in his summary, the author states that the Thomas splint still stands as the mainstay for external immobilization of most of the femur. He adds, however, that good facilities for plastering should be available, as the combination appears ideal for purposes of transport. The views of K. W. Starr on the surgical pathology of fractures are quoted. In the chapter on orthopædic surgery we read that in one representative series of cases forty-six patients with protruded intervertebral disk were operated on and that thirty-seven obtained dramatic relief. The best results were obtained among those patients whose pain was most severe. The technical instruction issued in the later days of the war is reproduced in full and we are reminded of the special delegation in orthopædics (F. H. McC. Callow, B. T. Keon-Cohen and J. M. Jens) which reported to the armed services and the Repatriation Commission on the work done abroad and on the requirements in Australia. The delegation's report, published later, included a summary of the indications for various kinds of amputations. The history of the amputations that had to be undertaken in the various Japanese-controlled prison camps to relieve the sufferings of men with so-called tropical ulcers of the legs has been told in this journal and is familiar to readers. In the chapter on head injuries stress is laid on the gap that exists in the liaison between civil life and reemployment in the last phase of readjustment of these patients to everyday life. The details of the development and organization of plastic surgery in the Australian Army Medical Corps are to be told in another volume; in this volume reference is confined to such aspects as outline the history of the work and indicate its influence on war surgery. The training at special units of D. Officer Brown, B. K. Rank and K. W. Starr as surgeons and of A. J. Arnott as dental surgeon is mentioned. The author states that the work of plastic surgery has reflected on the outlook of other branches of surgery in numbers of ways. "Its teaching function has been active and important, and hardly less has been the example of its necessarily meticulous and detailed records, by which the progress of the art and science of plastic surgery can be measured." In the chapter on anæsthesia it is stated that there is no doubt that the work of specialist anæsthetists under service conditions has enhanced interest and raised standards in anæsthesia.

In the third part of the book devoted to special subjects there are nine chapters dealing with medicine and surgery in captivity, dental surgery, dermatology, oto-rhino-laryngology, ophthalmology, pathology, radiology, psychiatry, and medical rehabilitation. We do not propose to describe these; those who handle this book will naturally wish to see what the author has to say about these subjects. Particular attention is directed to the chapter on psychiatry, which opens with an appropriate quotation from Burton's "Anatomy of Melancholy": "It is a disease of the soul which I treat, and as much appertaining to a Divine as to a Physician." The chapter on medical rehabilitation has as a heading some words of T. S. Eliot: "Where is the penny world I bought?" To the author's epilogue reference is made elsewhere in this issue.

The scope of this volume has been indicated. A word must be added about the illustrations. They are first rate and there are 73 of them, as well as 15 maps and diagrams. The printing and general arrangement of the book leave nothing to be desired; the printers, the Advertiser Printing Office, Adelaide, are to be warmly congratulated on their product. In recommending this book to the careful attention of every medical man and woman in Australia, we would refer them to the leading article in this issue in which the significance of the work is discussed.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Medical Clinics of North America"; 1952. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Los Angeles Number. 9" × 6", pp. 300, with 45 illustrations. Price: £7 5s. per clinic year in cloth binding, and £6 per clinic year in paper binding.

Contains a symposium of 21 articles on recent advances in medicine.

"Studies in Visual Optics", by Joseph I. Pascal, B.S., M.A., O.D., M.D.; 1952. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9" × 6", pp. 800, with 138 text figures. Price: £6 11s. 3d.

The author's purpose is to present some old material in an effective way, as well as some new ideas and methods.

"Synopsis of Genitourinary Diseases", by Austin I. Dodson, M.D., F.A.C.S., and Donald L. Gilbert, M.D.; Fifth Edition; 1952. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 8" × 5", pp. 314, with 122 illustrations. Price: £2 2s.

For the use of the medical student and as a handy reference for the general practitioner.

"Surgery for Nurses", by James Moroney, M.B., Ch.B., F.R.C.S. (England), L.R.C.P. (London), with a foreword by Miss Dorothy M. Smith, O.B.E.; Second Edition; 1952. Edinburgh and London: E. and S. Livingstone, Limited. 9" × 6", pp. 688, with 585 illustrations. Price: 27s. 6d.

Extensively revised since the first edition was published in 1950.

"The Extra Pharmacopœia (Martindale): Incorporating Squire's Companion", published by direction of the Council of the Pharmaceutical Society of Great Britain; Twenty-Third Edition; Volume I; 1952. London: The Pharmaceutical Press. 7½" × 5", pp. 1374. Price: 55s.

A new edition of a standard reference book after a gap of eleven years.

"The Principles and Practice of Medicine: A Textbook for Students and Doctors", by L. S. P. Davidson, B.A. (Cantab.), M.D., F.R.C.P.Ed., F.R.C.P. (London), M.D. (Oslo), and the staff of the Department of Medicine and associated clinical units of the University of Edinburgh: 1952. Edinburgh and London: E. and S. Livingstone, Limited. 9" × 6", pp. 930, with 57 illustrations. Price: 32s. 6d.

Prepared primarily for the authors' students.

"The Microbiological Assay of the Vitamin B-Complex and Amino Acids", by E. C. Barton-Wright, D.Sc., F.R.I.C.; 1952. London: Isaac Pitman and Sons, Limited. 9" × 6", pp. 190, with 25 text figures. Price: 27s.

Each assay is described in detail.

"Medical Mycology: An Introduction to its Problems", by G. C. Ainsworth, B.Sc., Ph.D., F.L.S.; 1952. London: Isaac Pitman and Sons, Limited. 9" × 6", pp. 114, with eight plates and seven text figures. Price: 22s. 6d.

An attempt to provide an introduction to medical mycology by using the principal mycoses affecting man to illustrate general problems of the subject.

"Connective Tissues: Transactions of the Third Conference, February 14-15, 1952, New York", edited by Charles Ragan; 1952. New York: Josiah Macy Junior Foundation. 9½" × 6", pp. 166, with 50 illustrations, two in colour. Price: $3.50.

Papers with discussion are presented on connective tissue staining, the fine structure of connective tissues, the nature of reticulin and hypersensitivity and the hyperadrenal state.

The Medical Journal of Australia

SATURDAY, DECEMBER 13, 1952.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE AUSTRALIAN MEDICAL HISTORY OF THE WAR.

THE publication of Dr. A. S. Walker's first volume of his group of four in the Medical Series of the Australian History of the War of 1939-1945 is one of the most important events in Australian medicine of recent years. It is true that this is only the first of four volumes in a series, but as a forerunner it heralds the advent of the other three in not too long a time. When all four volumes have appeared the true perspective of the work of the medical services in Navy, Army and Air Force will be made possible. In the meantime we have presented to us a first-class account of the clinical problems that arose and of what was done towards their solution. Those who read the account—and we hope that they will be many—will recall the hopes of the periods in which medical advances were announced, and although Dr. Walker denies that the volume is a text-book, will probably learn more than they would from a book so described. They will realize that the outlook of the administrative staff in the second World War was essentially different from that of the first conflict. In the third volume of his medical history of the first war the late A. Graham Butler records that there were certain leading members of the Royal Army Medical Corps to whom all "science" was anathema. One of them declared that there was to be "no b———y research". This phrase became famous by the letters "N.B.R.". Butler shows that it was not only the Royal Army Medical Corps which adopted this attitude. The army itself was both short-sighted and obstinate. He gave examples to prove his contention. Butler records the Australian attitude. The Australian story was not quite so pathetic as the British. Butler writes of Surgeon-General Howes: "Fully alive through the Gallipoli experience to the practical importance of preventive medicine in the field, he was yet incapable of appreciating from his own experience the value of research as applied to the medical problems of this war." Lieutenant-Colonel A. H. Tebbutt, who was pressing the matter, was at length appointed adviser in pathology, and from then on all went well. Butler explains that Howse's attitude was very far from that of the "N.B.R." of the Royal Army Medical Corps. What strikes the reader at once about Dr. Walker's book is that it is a continuous record of work carried out by medical officers of the three services. Throughout the conflict the heads of the medical services encouraged their officers to record experimental and clinical observations and directed most of them to this journal—that most of the references in the book are to this journal has been noted in the review. We may remark in passing that the journal became an important instrument for the services and also forged one of the links between medical personnel on active service and those who were cast for service at home, in civil practice. Members of the community do well to remember that the medical profession was the only group of the community which virtually conscripted itself. This meant that the profession was not split into sections—it remained the single cohesive body that it had always been. In these circumstances the existence of links between doctors at home and abroad was of vital importance. But we must return to the question of research in the services. Readers scarcely need to be reminded that the medical heads did not stop at encouragement to report observations made in the laboratory or elsewhere; the planned malarial research at Cairns, which may well be described as epoch-making, should alone dispose of any such suggestion. For information on work in pathology the reader is referred to the chapter on that subject in the "Special Subjects" part of the book. Dr. Walker is, of course, quite right when he states that there is in one sense little to write about clinical pathology *per se* in relation to everyday medical and surgical work during the war, because it is "inextricably woven into the fabric of modern medical practice". He points out that, although it is not always possible to have the pathologist available in forward areas, his influence still pervades the work done there. From the time when training was beginning in the Middle East, fully equipped pathological departments were part of the establishment of hospitals, and mobile bacteriological laboratories also provided full services. Reference might be made to pathological work carried out for the services in civil hospitals, in government laboratories, at universities and at research institutes, but this is not necessary. It must be quite obvious that right from the start the service chiefs adopted the correct policy—the cry of "N.B.R." had been outmoded long ago.

In looking at this volume as one of a group of formal histories, we may remember that the historical method has been described as comprising four processes. First of all facts have to be got together; secondly, these facts have to be arranged according to the factors of time and causation; thirdly, they have to be criticized, chiefly in order that their value may be learned; and fourthly, some

kind of interpretation has to be given to them. This has recently been expressed in another way by a writer in *The Times Literary Supplement*—the historians have not merely to present and explain the past; they have to contribute towards a better conduct of the future. This is a great responsibility to place on the shoulders of a war historian, or so it seems, but if his facts are right, and he has a sound and wide philosophical outlook, his interpretations should not be lacking in wisdom. Looked at with these ideas in mind, "Clinical Problems of War" must receive high praise and commendation and its author the warmest possible congratulations. In this book we must not expect too much in the matter of interpretation or contribution to a better future. This is the first of four volumes and it deals with clinical problems only; the work of the medical services in the different theatres of war, the movements of units and the achievements of their personnel have yet to be related. We may look forward with confidence to the contents of the next three volumes. In the present instance the reader will find Dr. Walker's "interpretations" right and he will not be disappointed in the epilogue. This is a book about the problems which Australian doctors had to face in war; Dr. Walker has shown by their writings how the Australian doctors solved their problems. Right through the work he makes comments when they appear to be needed either on the significance of some achievement in the medical conduct of the war or on its value in ordinary civilian practice. In the epilogue two serious questions are raised. The first has to do with the organization of medicine in peace time for the good of the community. In social and industrial medicine, which follow the call of both science and humanity, much more is needed. "The problem is to find how this can be done without sacrificing standards of work, and without stirring to wakefulness the lightly sleeping demons of avarice, slothfulness and strife." As the citizen receives greater benefits from the State, so is his life more bond than free. The individual becomes more frustrated and so more aggressive; this is well seen in service medicine. The individual relationship of doctor to patient was often difficult to preserve. Dr. Walker thinks that already there are signs that these ties are slackening in civil communities. In his opinion it seems unlikely that the physician-priest will ever become extinct, but he asks whether there is not a danger that he may become obsolete. The second question raised turns attention to the beckoning finger of science. Here the following words are significant:

> During the years of war we owed a vast debt to science, with whose gifts we wrought not only good but evil. In the war story of the medical services the need for scientific direction is apparent; so, too, is the need for humility. But now we know we cannot go back, and in going forward whither are we going? Even in the field of medical science shall we go on and on to more rarefied atmospheres of applied knowledge where humanity with its warm spiritual metabolism will faint and die? Science is not enough, nor will it avail to evoke the restraining of history and experience. Man is blind to experience, and deaf to history. As always he is intoxicated by power, and the new heady brews of scientific method are leading him more and more to destroy, not only by the physical violence of wrecking and killing, but by the moral violence of suppressing and denying the true culture of mind and spirit. Should we not look to ends rather than to means? Nothing but a change of heart can do this, for it is a question of spiritual values. The doctor is still a champion of the individual; he stands at the springs of life and death in peace as in war, and as a citizen he must accept this challenge.

Current Comment.

THE SINGLE CASE REPORT.

THE value of a single case report cannot be denied, for by this means many advances and many "new" syndromes have been recorded for the first time. William Beaumont wrote a book of outstanding importance on the case of Alexis St. Martin, but reference to R. H. Major's "Classic Descriptions of Disease" reveals several other instances of a less striking character—Cadwallader's "extraordinary case in physic" (osteomalacia), Fröhlich's syndrome, Henoch's purpura and Herrick's description of sickle cell anæmia, to name but a few. Cholecystectomy was introduced to the world by Carl Langenbuch's account of its successful performance in a middle-aged male. More than once, even in Australian medical literature, a physician has reported his own case for the benefit of his colleagues. In brief, some courage is necessary to criticize a form of medical writing for which there is precedent in the works of Hippocrates. Morgagni and Heberden; but L. E. Hines and D. L. Kessler[1] have drawn attention to the pitfalls of the method—in a single case report entitled "The Whimsy of a Single Case Report". They quote at length the case history, as it was presented to a hospital staff conference some time previously, of a male adult who developed an epileptiform seizure six days after the administration of penicillin, followed two or three weeks later by urticaria. The patient, a hay fever subject, had suffered in the past from dermatitis and giant urticaria following sulphonamide and penicillin therapy respectively. On examination, some abnormal neurological signs confined to the right side were elicited. An electroencephalogram showed evidence of an irritative focus in the left temporal region. The case was presented as the first reported example of allergy to penicillin producing angioneurotic œdema of the brain leading to an epileptiform fit. In an addendum, Hines and Kessler state that the patient, present at the meeting, was recognized by another physician as one of a family of known epileptics. When taxed with this, the patient became angry at the revelation of his secret and refused further treatment. Hines and Kessler point out that the story illustrates the danger of basing extravagant conclusions or claims on an isolated case, and that there is a risk that these may be accepted without question by the uncritical reader. They support their contention by reference to recent American papers of this nature. Their argument, therefore, is directed not against the single case report *per se*, but against the use to which it may be put.

Francis Bacon in "The Advancement of Learning" commended the wisdom and integrity of Aristotle, who "cast all prodigious narrations, which he thought worthy of recording" into a book separate from his main thesis, "excellently discerning . . . that rarities and reports, that seem incredible, are not to be suppressed or denied to the memory of men". One assumes that Hines and Kessler would attribute the same wisdom and integrity to modern medical editors who universally adopt a similar practice.

THE HAZARD OF INHALATION DURING ORAL SURGERY.

THE frequency with which tonsillectomy and dental extraction are performed and the gravity of the occasional complications, which are to some extent preventible, have led more than one forensic pathologist to regard these operations as amongst the most dangerous in surgery. Although the transient bacteriæmia following the pulling of a single tooth may give rise to an endocarditis of valves previously damaged by rheumatic fever, the out-

[1] *Surgery, Gynecology and Obstetrics*, July, 1952.

standing complications result from the aspiration of blood or other material from the oro-pharynx. It may be recalled that seven of a series of 51 deaths during anæsthesia reported in two articles by K. M. Bowden and by E. Gandevia in this journal three years ago[1] occurred during tonsillectomy or dental extraction, and that six of these deaths were asphyxial. In three cases inhalation of blood into the trachea and bronchi had taken place. It is not difficult to envisage the development of a lung abscess as a later complication had any of these patients had the good fortune to survive.

The problem of the inhalation of foreign material during oral surgery has been carefully studied by G. W. Scott,[2] of Guy's Hospital. His paper is commended to all who are concerned in such work, particularly as it contains much information which does not lend itself to summary. Post-operative radiographs showed that inhalation of radio-opaque oil (injected into the mouth during the extraction, in amounts of one to three millilitres) had occurred in 25 of 100 consecutive cases in which nitrous oxide was given to patients while seated in the dental chair. Evidence is produced to indicate that the chief factors favouring inhalation were head retraction, inefficient packing of the oro-pharynx and multiple extractions, especially if including back teeth. Scott points out that the sitting position has been discarded for tonsillectomy because of the high incidence of subsequent pulmonary abscess, but that it is still in general use for dental extractions. In a series of 50 cases in which the patient was operated on while lying on a table with the head and thorax lowered 30° from the horizontal, inhalation of oil was noted in only one case; although, as Scott stresses, the two series are not comparable in some respects. A follow-up study of a total of 150 cases revealed that 33 patients developed coughs or colds but showed no abnormality radiologically. The significance of this finding is impossible to assess in the absence of a series of controls. However, one patient developed an area of pneumonitis in the lower lobe of the right lung where the presence of radioopaque oil had been demonstrated immediately after operation. The low incidence of radiologically demonstrable infection, compared with the incidence of inhalation, is attributed to the careful attention paid to improvement of oral hygiene before extraction was attempted. It is interesting to note that children appeared less liable to aspirate the oil, and that inhalation of oil occurred occasionally when the extraction was performed under local anæsthesia. Scott is careful to draw attention to the possible sources of error in the method and in the interpretation of the results.

The essential feature which emerges is that a reduction in the morbidity and mortality of oral surgery may be effected by meticulous attention to well-established dental and anæsthetic principles. Scott's demonstration of the effectiveness of adequate packing and the adoption of the horizontal position in reducing the incidence of inhalation of even minute quantities of the oil suggests that in most instances there is little excuse for the inhalation of sufficient blood to produce an asphyxial death.

THE CLINICIAN AND CLINICAL RESEARCH.

THE term "clinical research" is so broad as to defy accurate definition, but Sir Cecil Wakeley[3] has aptly observed that its essence lies in the fact that it is "carried out by the clinician—be he general practitioner or specialist—and it is research on the 'human animal' during the course of his normal health or during illness". It is an unfortunate misconception that this work should be the prerogative of the professorial unit or the specialist team. Sir Cecil Wakeley stresses that the general practitioner, by virtue of his long association with his patients, both in sickness and in health, possesses a distinct advantage in many fields, notably, perhaps, in regard to the long-term assessment of rehabilitation measures and the problems of geriatrics. Lack of special investigations should prove no bar to progress in many instances, but nevertheless they offer further facilities to doctors associated with a hospital. *The Lancet*, in a leading article[1] drawing attention to Sir Cecil Wakeley's address, observes that the efficiency of hospital services would be greatly enhanced if the clinician undertook such work in addition to his routine duty of treating his patients. It may be noted that the honorary medical officer has at his disposal a proportion of the time of his junior associates, the precise proportion available for research being largely dependent upon the stimulus and inspiration which he provides. The problems investigated need not be of great complexity—the efficacy of a drug, dressing or nursing procedure, the significance of a symptom or sign, the normal variation of fluid intake or body weight, are all capable of some elucidation without resort to elaborate techniques. In a broad consideration of the role of clinical research in a voluntary teaching hospital, Owen H. Wangensteen[2] emphasizes that the starting point is usually an accurate observation coupled with the realization that it is neither trivial nor incidental. An intelligent patient, suffering from recurrent attacks of pyrexia of unknown origin, recently noticed that his finger-nails became ridged longitudinally during each bout of fever, and that these ridges disappeared as the nails grew in the symptom-free intervals. This observation must have some significance, and it is not beyond the capacity or the facilities of anyone interested to investigate the phenomenon further. Wangensteen would agree that expert assistance may be invaluable in designing a crucial experiment to give a definitive answer to a question, for here, as he points out, specialized training and knowledge may prove indispensable. Wangensteen considers that the enthusiasm of a teacher for his subject and the force of his example are two of the great catalysts of a university education. The cultivation of a scientific outlook in the student is best achieved by permitting him to see, and perhaps take part in, clinical research of this nature, rather than by offering him a series of didactic lectures in the scientific method, which he finds applied only on a large scale in certain special units.

With humour and understanding, Professor A. Bradford Hill,[3] in an address at Harvard Medical School, has outlined the relationship between the statistician and the clinician in clinical research, and the role of each in the planned, controlled clinical trial. Having quoted Sir Henry Dale's dictum that "all true measurement is essentially comparative", he proceeds to discuss in non-technical terms the need for a control group, the methods of random allocation and the precautions necessary to avoid bias or, sometimes more important, the accusation of bias. Essential preliminary steps are the posing of clear questions to which answers are required and the planning in advance of the measurements to be taken. Professor Hill illustrates the importance of the latter point by reference to an old statute which enacted that one-half the penalties under the Act were to be given to the poor of the parish and one-half to the informer, yet subsequently the only penalty prescribed was fourteen years' transportation to the colonies, for which, doubtless, neither party was grateful. He does not omit to answer the criticism that "the replacement of humanistic and clinical values by mathematical formulæ" results from the employment of the statistical method. In effect, he has drawn on his wide experience with the Medical Research Council and other institutions to provide a valuable introduction to the statistical approach to clinical research; to those who fear or distrust it and to those whose time is limited, but whose interests extend beyond "the routine care of patients", his paper is commended.

[1] THE MEDICAL JOURNAL OF AUSTRALIA, January 22, 1949.
[2] *Guy's Hospital Reports*, Number 2, 1952.
[3] *British Medical Journal*, April 26, 1952.

[1] *The Lancet*, May 3, 1952.
[2] *The New England Journal of Medicine*, June 19, 1952.
[3] *The New England Journal of Medicine*, July 24, 1952.

Abstracts from Medical Literature.

THERAPEUTICS.

Dicoumarol Therapy for Acute Myocardial Infarction.

IRA A. RASHKOFF, LOUIS E. SCHAEFER, MELVILLE G. MAGIDA AND HYMAN LEVY (*The Journal of the Mount Sinai Hospital*, March-April, 1952) present an evaluation of dicoumarol therapy in 287 cases of acute myocardial infarction. The patients were carefully selected from among patients in hospital surviving more than twenty-four hours; 142 received dicoumarol and 145 served as controls. Except for the use of anticoagulants in the one group, treatment in both groups was essentially the same. The dicoumarol dosage was 300 milligrammes on the first day and 200 milligrammes on the second day of treatment in hospital. The prothrombin time served as a daily guide to further doses, the objective being to maintain the prothrombin time at a level between two and two and a half times the control, that is, twenty-five to thirty seconds. The dicoumarol therapy was continued till the patient was ambulatory, which was, on the average, after five weeks. The death rate in the dicoumarol group was 13%, and in the control series it was 27%. The incidence of thrombo-embolic complications was 14% in the dicoumarol group and 26% in the control series. Death was associated with clinically evident thrombo-embolic complications in only 4% of cases in the dicoumarol group, in comparison with an incidence of 10% in the control group. A pronounced reduction in the mortality rates in all age groups was noted among those receiving dicoumarol. The administration of the drug produced eight instances of minor hæmorrhagic complications, and an additional case in which death without apparent hæmorrhage may well have been due to the use of dicoumarol. The authors state that the study supports the conclusion that patients with acute myocardial infarction should be treated with anticoagulants as a routine except when recognized contraindications are present.

Amœbicidal Drugs.

W. A. SODEMAN AND P. C. BEAVER (*The American Journal of Medicine*, April, 1952) report a study on the relative efficacy of two well-known amœbicidal drugs, "Diiodoquin" and "Chiniofon", and two newer drugs, "Milibis" and "Thioarsenites", that had not at that time been given extensive clinical trial. The efficiency of "Milibis" and "Thioarsenites" in cases of *Entamœba histolytica* infection was of high degree, and the authors state that their results confirm the efficacy of these drugs against other amœbæ. Results were also uniformly good with "Diiodoquin", but "Chiniofon" appeared to be less effective.

Prophylaxis of Seasickness.

H. I. CHINN *et alii* (*The American Journal of Medicine*, April, 1952) report the results of trial of various drugs in the prophylaxis of seasickness. They state that no preparation was significantly superior in its effect to diphenhydramine ("Benadryl"), although the observed percentage of protection afforded by phenothiazine hydrochloride ("Lergigan") was slightly greater. Certain antihistamine drugs gave no protection. Side effects were minimal in all cases except among persons receiving scopolamine aminoxide; two milligramme doses of this given three times a day caused hallucinations, an increased incidence of nightmares, dry mouth, blurred vision and ringing in the ears. When one milligramme was combined with 25 milligrammes of "Benadryl", there were no hallucinations, but the incidence of nightmares, dry mouth and blurred vision was still increased.

Thiopentone Reactions.

F. LEMERE (*Anesthesiology*, January, 1952) describes a series of 1027 cases of chronic alcoholism in which treatment was given, *inter alia*, with sodium thiopentone; each patient received an average of fifteen administrations. He states that the well-known immediate complications that occurred were vomiting, cessation of respiration, coughing and choking from laryngeal spasm, convulsions, nervous tension on the following day and venous thrombosis. Delayed reactions which were encountered were fever up to 104° F., arthralgia, skin rashes, weakness and general malaise for up to five days. These reactions were considered allergic in nature, and all responded to administration of ACTH, 25 to 50 milligrammes being given immediately and 25 milligrammes every eight hours.

Transfusion Reactions.

J. E. OSBORN AND T. H. SELDON (*Current Researches in Anesthesia and Analgesia*, January-February, 1952) studied 591 patients who underwent 2260 transfusions in order to determine the frequency of reactions in multiple transfusions. The reaction rate for the first transfusion was 7·3%; 5·3% of the remainder developed reactions after the second transfusion, 5·2% after the third, 6·3% after the fourth and 9·0% after the fifth. Among those who developed a reaction during the first transfusion, the reaction rate for the second transfusion was 27·9%. The age of the blood, sex and blood group had no significant effect on the reaction rate. Most of the reactions were pyrogenic.

Chlorophyll and Hospital Odours.

L. J. LE VANN (*The Canadian Medical Association Journal*, July, 1952) states that the objectionable smells associated with the nursing of low-grade mental defectives were considerably reduced by giving the patients chlorophyll tablets, in a dosage of 100 milligrammes twice a day.

Sciatic Nerve Block.

MILTON J. MARMER (*Anesthesiology*, March, 1952) presents a series of 53 nerve blocks to compare the effects of sciatic nerve block and paravertebral lumbar sympathetic ganglion block in the treatment of peripheral vascular disease. His concept is based on the fact that the sympathetic nerve supply to the vessels of the extremities is carried mostly by the somatic nerves and not by the arterial plexus. He states that sciatic nerve block caused a greater and more certain rise in temperature of the foot than paravertebral lumbar sympathetic ganglion block, there were no complications, and there was much less discomfort to the patient. Two patients with intermittent claudication were treated successfully with sciatic nerve block. Procaine and "Metycaine" were the local anæsthetic agents used in the series.

Vitamin A Intoxication.

G. C. RYERSBACH, J. HANELIN AND R. J. JOPLIN (*The New England Journal of Medicine*, June 19, 1952) report a case of vitamin *A* intoxication in a three-year-old girl. The child had been taking 240,000 units of vitamin *A* per day for approximately one year. She presented with soreness of the forearm and hip without redness or swelling. The pain was so severe as to prevent walking. For three months there had been an itchy red rash all over the body and cracking and bleeding of the lips. She had been irritable and anæmic, and the hair had commenced to fall. Examination showed poor physical development, thick diffusely erythematous skin, cracked dry lips and sparse dry hair. Tender swellings could be palpated over the lateral aspects of the right leg. There was a very high vitamin *A* blood level. X-ray examination showed widespread subperiosteal new-bone formation. There was rapid improvement upon stopping the intake of vitamin *A*. Within one year the skeleton was normal.

"Probenecid" and Serum Penicillin Concentration.

A. R. FRISK, N. DIDING AND G. WALLMARK (*The Scandinavian Journal of Clinical and Laboratory Investigation*, Volume IV, Number 2, 1952) discuss experimental observations on "Probenecid", a benzoic acid derivative. They state that this substance inhibits the renal tubular excretion of penicillin in the same way as carinamide, but is effective in small doses and has a low toxicity. The study was in part devised to determine to what extent the combination of "Probenecid" and oral penicillin therapy could replace parenteral administration of penicillin. It was found that a dosage of 500,000 units of penicillin and 1·0 gramme of "Probenecid" every eight hours ensured a minimum serum penicillin level of 0·1 unit per millilitre. The results indicated that this dosage every eight to twelve hours would be adequate for the treatment of the majority of infections caused by penicillin-sensitive organisms. Also, for intensive penicillin therapy, the combination of "Probenecid" and large intramuscular doses of penicillin was thought highly effective. The authors conclude that "Probenecid" in conjunction with oral penicillin treatment is of the greatest practical value.

Angina Pectoris.

R. C. SCOTT AND V. J. SEIWERT (*Annals of Internal Medicine*, May, 1952) discuss the treatment of *angina pectoris* with pure crystalline khellin, the name given to 2-methyl-5,8-dimethoxy-furano-chromome. The compound was previously called visammin. Tablets of 50 milligrammes were given four times daily. Seven patients out of 14 became nauseated on a dosage of 200 milligrammes per day. Some of these patients were not nauseated on a dosage of 100 milligrammes per day. Eight patients had fewer anginal

attacks while under treatment. Six showed no improvement. Three patients showed improvement in exercise tolerance after khellin therapy. Duration of treatment was from five to twenty-nine days. Other side effects were polyuria, weakness and anorexia. The authors consider crystalline khellin less toxic than khellin mixtures. The benefits recorded are regarded as rather small, considering the number of toxic effects.

ACTH, Cortisone and Tuberculosis.

A. W. CAPON (*The Canadian Medical Association Journal*, July, 1952) reports two cases which add to the evidence that ACTH and cortisone act adversely on tuberculous infection. In the first, tuberculous pus was aspirated from an axillary gland and from the shoulder joint after treatment of scleroderma and dermatomyositis with cortisone. In the second the patient, who had disseminated *lupus erythematosus*, improved with cortisone, but then became very ill with miliary spread of tuberculosis through the lungs and to the meninges.

NEUROLOGY AND PSYCHIATRY.

Restoration of Motor Function after Hemiplegia.

THOMAS E. TWITCHELL (*Brain*, Volume LXXIV, Part 4, 1951) describes in detail studies on 25 patients affected with hemiplegia, chiefly of vascular origin. Periodical clinical and electromyographic studies were employed in all cases from time of admission to hospital up until a reasonably stable condition had been reached. The author states that there was a remarkable uniformity in the steps of recovery in the different cases and that restoration of motor function in all cases followed a general pattern, in which the recovery process had halted at various points in each case. He concludes that this regular sequence of changes is reflex, and that each change is associated with an increase in ability for voluntary movement. The process of recovery may become arrested at any stage in this sequence. The initial phase is one of depression of all motor function, and during it all proprioceptive responses are hyperactive. These proprioceptive responses are modified in their turn by other factors (such as stretching of associated muscles or alteration in the position of the patient's head in relation to the body). As the recovery proceeds, the more primitive proprioceptive responses become subordinated to special exteroceptive stimulation. Voluntary movement appears as a further facilitation of the available responses at each stage and is not a separate entity. From its first appearance, voluntary movement takes the form of conditioned proprioceptive and contactual responses.

Boeck's Sarcoid with Central Nervous System Involvement.

WILLARD H. PENNELL (*A.M.A. Archives of Neurology and Psychiatry*, June 1, 1951) describes three cases of sarcoidosis with central nervous system involvement. From them he has made the following conclusions. Sarcoidosis, as a low-grade chronic disease of unknown origin, may involve any part of the central nervous system with a multiplicity of symptoms. There have been 51 such cases reported in the literature. The commonest symptom of involvement of the nervous system is *diabetes insipidus*; other complications include visual loss, convulsive seizures, confusional states, hemiplegia, cerebellar and sensory signs, and papilloedema. There may be a low-grade meningeal reaction with a lowering of cerebrospinal fluid sugar content, which the author considers to be a point suggesting an infectious origin for Boeck's sarcoid.

Altered Consciousness and Brain-Stem Lesions.

MICHAEL JEFFERSON (*Brain*, Volume LXXV, Part 1, 1952) reports six clinical cases of brain-stem lesions affecting chiefly the mesencephalic tegmentum. A feature of all these cases, apart from the other signs, was a varying degree of disturbance of consciousness ranging from drowsiness to coma. The author states that the maximum impact of the disease fell upon the mid-brain tegmentum, although the diagnosis could not be confirmed by autopsy as all six patients recovered. Three patients had an angiomatous malformation of the intrinsic vessels of the brain stem; another was thought to have an aneurysm of the basilar artery and one an embolus in the basilar artery. The discussion arising from these cases centres round the exact anatomical location of the lesion likely to cause changes in consciousness. The author mentions Bremer's theory that in parasomnic cases interruption of the great sensory pathways occurs, with consequent deafferentation of the cerebral hemispheres and removal of all sensory stimuli thought responsible for the waking state. However, this theory has been questioned by Magoun and his colleagues. Experiments carried out on animals with chronic lesions in the reticular substance of the tegmentum of the mid-brain and upper part of the pons have shown that the reticular substance plays a cardinal role in the preservation of wakefulness, by offering a constant excitation directed toward the hemispheres, and in a roundabout fashion by virtue of its facilitatory effects upon lower motor channels. Magoun infers that the great sensory tracts of the brain stem are important only in so far as they provide collateral channels by which the action of the reticular formation may be enhanced. The author concludes that, in the light of this new knowledge, it could be suggested that the parasomnias associated with brain-stem lesions indicated some involvement of the reticular formation

Pulsatile Cells in the Brain.

C. M. POMERAT (*The Journal of Nervous and Mental Disease*, November, 1951) describes pulsatile activity of cells from the human brain in tissue culture. His data are taken from 8000 cultures made from tissues from 121 patients, 47 of whom had intracranial tumours. Cinematographic records were made from cultures at body temperatures. The article is fully illustrated. Three varieties of pulsatile cell types are described—cells with globose cell bodies, cells with vase-shaped or pear-shaped bodies, and cells with multibranched processes. The time for one pulsation was found to vary from eight to twenty-three minutes. Based on studies in the cat, the suggestion is made that pulsatile types of cell can occur in the peripheral nervous tissues. The author suggests that the function of pulsation may be to move tissue fluids, and that it may contribute to findings in the electroencephalograph.

Glutamic Acid and Mental Deficiency.

K. ALBERT, P. HOCH AND H. WAELSCH (*The Journal of Nervous and Mental Disease*, December, 1951) have made a comprehensive survey of the effect of glutamic acid on 148 mental defectives over four years of administration. Controls were provided by giving the drug for four-monthly periods followed by an equal period in which a placebo was given. Intelligence tests were made after each period. The psychologist did not know whether it was the drug or the placebo session. At the conclusion 70 defectives had completed the entire course, and it was felt that the results warranted statistical appraisal. The patients' improvement was checked by reports of a social worker, and the parents were encouraged to come with their children. A highly significant change in intelligence quotient as a result of glutamic acid administration was found ($P < 0{\cdot}001$). This was based on children with a low intelligence quotient, since those in the higher group usually failed to complete their treatment. The results in 50 cases were statistically unavailable. The authors found the best results in cases of secondary amentia, though mongols also derived much benefit. They suggest that the results may be due not so much to the intellectual performance as to the use of existing intellect. Glutamic acid stabilizes the emotion and so permits better use of the environmental and emotional components.

Intraventricular Medication in Catatonic Stupor.

STEPHEN L. SHERWOOD (*Brain*, Volume LXXV, Part 1, 1952) discusses the effects produced upon three subjects of catatonic stupor by intraventricular injection of the drugs cholinesterase, procaine, pentamethonium iodide and "Flaxedil". He states that recent observations suggest that the autonomic centres are profoundly involved in several forms of mental illness, and that in certain forms of mental illness they may actually be the seat of the disease. A working hypothesis is suggested, namely, that certain mental diseases correspond to a state of pathological autonomic imbalance, probably within the diencephalon. If this hypothesis is correct, the improvement in persons suffering from certain mental diseases after leucotomy may be due to interruption or suppression of activity among the diencephalic centres. The author suggests a more accurate and less mutilating method by which the drugs are administered locally. In a test case injections were made into the frontal horn of the lateral ventricles through burr holes in three patients. With the first patient all four drugs were used, with the second all drugs except procaine, and with the third "Flaxedil" and pentamethonium iodide only. The effect aimed at was relief of the catatonic stupor. With all three patients this effect was achieved to some extent; it was greatest with cholinesterase in the first patient, and with pentamethonium iodide in all three patients.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XLV.
COLLES'S FRACTURE.

COLLES'S FRACTURE of the carpal extremity of the radius was first described by Abraham Colles in the *Edinburgh Medical and Surgical Journal* in 1814, and whereas Colles considered the fracture to occur approximately one and a half inches from the distal end of the radius, later observations and X-ray examination have shown that the fracture is usually about one inch from the articular surface. Furthermore, Colles described only the simple fracture and omitted reference to the comminuted fracture, which is of frequent occurrence.

A brief description of this fracture is as follows. As a result of a fall on the outstretched hand, the distal extremity of the radius is fractured either more or less transversely or into two, three or more fragments, approximately one inch from the carpal articular surface of the radius. The distal fragment or fragments angulate dorsally and radially in such a way as to produce the typical dinner-fork deformity as seen in most cases. This foreshortening of the radius causes the head of the ulna to become more prominent on the ulnar and volar aspects of the wrist. The styloid process of the ulna may be avulsed in part or in whole as a result of the force which caused the hand to deviate radially. In some cases the force is so great that the styloid process or head of the ulna ruptures the overlying skin and converts (from within) a closed fracture into a compound one. In rare instances the distal end of the large proximal fragment of the radius penetrates the skin on the volar aspect of the forearm, and in such cases the tendons, nerves and large vessels usually escape serious damage.

In children, the same injury is represented by a similar displacement of the distal epiphysis of the radius.

The rather common transverse fracture of both radius and ulna approximately two inches above the wrist joint with complete dorsal displacement of the distal fragment of the radius must not be confused with a Colles's fracture in the case of children, as reduction of that fracture is rather more difficult and demands a different technique, although the method of splinting is similar to that of a Colles's fracture.

In the matter of the differential diagnosis, dorsal dislocation of the carpus should not be mistaken for a Colles's fracture if the examination is made before much soft-tissue swelling has occurred.

Treatment.

An X-ray examination should be made in every case of suspected fracture, even in the absence of deformity, as frequently fissure fractures occur and require treatment.

In the case of a compound fracture, wound toilet, *débridement* and antibiotic insufflation, reduction of the fracture, and immobilization, should be carried out with due aseptic precautions within six hours of the receipt of the injury.

The closed fractures, especially those associated with severe deformity, should be reduced and splinted before secondary soft-tissue swelling becomes pronounced, otherwise redisplacement is prone to occur and the skin develops blebs and blisters, and splinting becomes difficult.

When it is at all possible, reduction should be carried out on an X-ray table so that the position can be checked and corrected if necessary. This procedure frequently obviates the need for several anæsthetics, and ensures a more satisfactory result and a more satisfied patient.

The actual manipulation of the fragments should not be carried out during the X-ray exposure, as this endangers both the patient and the surgeon to X-ray burns.

Reduction of the fracture is facilitated if firm countertraction is provided by a roller towel passed around the upper part of the arm just above the elbow, with that joint flexed to a right angle and the arm abducted to a right angle at the shoulder; the roller towel is then tied to some rigid structure at the head of the table.

The method of reduction varies somewhat with the type of fracture undergoing treatment.

In the case of the simple transverse fracture, when the right forearm is affected reduction is readily achieved by the surgeon by placing the butt of his left hand over the volar aspect of the proximal fragment close to the line of fracture, whilst the fingers of the same hand are wrapped around the ulnar side of the forearm. The butt of the surgeon's right hand is then placed over the dorsum of the small distal fragment, whilst the fingers of that hand grasp the patient's hand along its radial side. Traction is imparted by means of the right hand, firstly in a direction to increase the deformity slightly and momentarily, then in an ulnar direction to obtain full length of the bone, and finally volarwards to lock the fragments and reproduce the normal forward curve of the distal end of the radius.

In the case of a fracture of the left forearm, the surgeon's hands are reversed as regards their position in relation to the fracture.

Comminuted fractures, on the other hand, require countertraction by means of the roller towel as before mentioned; then the patient's hand is grasped and steady traction is applied in line with the forearm and somewhat ulnarwards. When full length has been obtained, with fingers and thumb the various fragments are gently manipulated into as good position as possible, then the forearm is supported and the patient's hand is lowered into about 30° of palmar flexion and full ulnar deviation.

Methods of Splinting.

The two types of splint most frequently used for immobilization of a Colles's fracture are aluminium gutter splints and plaster of Paris moulds.

In the case of a simple transverse fracture, aluminium gutter splints are efficient and comfortable if applied as follows: (i) a dorsal splint padded with felt, twisted in a spiral manner so as to follow the rotation of the pronated forearm and extending from elbow level to the heads of the metacarpals; (ii) a volar splint similarly padded and twisted to follow the rotation of the volar aspect of the forearm and extending from elbow level and to the line of the fracture. A small pad of cotton wool about one and a quarter inches wide and half an inch thick is placed across the volar splint at its distal extremity, and a similar pad is placed over the dorsum of the distal fragment before the dorsal splint is applied.

The two splints are held in position by either two strips of adhesive strapping or two lengths of tape, one at the proximal and one at the distal extremity of the volar splint. A pad of cotton wool is then placed between the dorsum of the hand and the dorsal splint, and a gauze bandage is used to encircle both splints and finally incorporate the hand loosely against the end of the dorsal splint.

Should the fracture be comminuted, or as an alternative to metal splints, plaster of Paris moulds provide excellent fixation. When the fracture has been reduced the forearm is pronated, the hand is held in about 30° of palmar flexion and in ulnar deviation, and a three or four inch plaster of Paris bandage is laid layer by layer on the dorsum of the forearm and hand in a spiral manner until the required thickness is obtained.

A volar slab of plaster of Paris is prepared and placed along the forearm from elbow level to the distal end of the radius; this slab should be broader at the proximal end, and there should be a gap of one-quarter or three-eighths of an inch between the dorsal and volar moulds on both the radial and ulnar sides after a gauze bandage has been applied around them; this bandage should also pass around the palm of the hand and the dorsal mould. As the plaster is setting, great care must be taken to mould the volar slab well into the curve of the radius at its distal end, whilst the dorsal mould should be curved around the radial side of the thumb and even around the radial side of the neck of the index metacarpal to prevent radial deviation of the hand. When the plaster has set, strips of adhesive strapping are used to encircle the moulds at either end, and a third piece is passed beneath the palm of the hand and over the dorsal slab.

Where there is danger of foreshortening of the radius owing to gross comminution, it is advisable to apply a third plaster mould from the proximal third of the forearm onto the lower half of the upper part of the arm anteriorly with the elbow at a right angle so as to immobilize the fracture site more securely. This mould is bandaged onto the forearm and upper part of the arm by means of a gauze bandage.

After Care.

If the fracture is splinted very soon after the injury, excessive swelling may occur and cause cyanosis and œdema of the fingers, in which case the splints must be loosened without delay. It is most important to see that the splints or plaster moulds are kept in firm contact with the forearm as the swelling of the wrist and forearm subsides. This is done by inspecting the limb every three or four days and applying fresh strips of strapping around the splints or by tightening the tapes which encircle the limb. If the splints are allowed to become loose on the limb, the fragments are readily displaced, and a poor result ensues. Immobilization must be maintained for five weeks, at the end of which time clinical examination may confirm good union; if one is in doubt, an X-ray examination should be made before the splints are dispensed with.

As soon as the patient recovers from the anæsthetic, he should be encouraged to move his fingers and thumb actively and to elevate and externally rotate the shoulder joint in order to minimize or prevent stiffness in those joints. Elbow movements may be commenced in ten to fourteen days in most cases.

Complications.

Stiff Fingers.

Stiff fingers may be the result of preexisting arthritis of the metacarpo-phalangeal and/or interphalangeal joints. The degree of residual stiffness is reduced by early active use of the fingers and avoidance of too firmly applied splints.

Excessive œdema of the hand resulting from tight bandaging will cause stiff fingers. This can be avoided by examining the limb frequently during the first week and adjusting the splints when necessary.

Sudeck's atrophy will cause stiffness of fingers and pain in the hand as a late complication in some cases. Treatment consists of the administration of cortisone and ACTH and active use of the limb.

Stiff Wrist.

A stiff wrist is usually the result of arthritis of that joint. The arthritis may precede the injury and be aggravated by the fall, or it may result from infection in the case of a compound fracture or follow a comminuted fracture in which the joint surface is fragmented.

Treatment of this condition consists of rest on a cock-up splint after the fracture has united, and avoidance of excessive use of the joint for many weeks.

Should pain and increasing stiffness persist, arthrodesis of the wrist may be necessary.

Other Complications.

Transitory stiffness of wrist and fingers may result from adhesions about the flexor tendons in the forearm in a few cases. Massage and active and passive movements are necessary to hasten recovery.

Pain about the head of the ulna is not infrequent when activity is resumed. This usually subsides gradually, although in some cases it persists for many months.

Restricted pronation and/or supination may be the result of incomplete reduction or of arthritis of the distal radio-ulnar joint.

Shoulder-joint stiffness is a frequent complication if the patient is not instructed to elevate and externally rotate the arm at the shoulder several times a day from the commencement. Physiotherapy is indicated when the stiffness is established, and not infrequently manipulation of the joint under general anæsthesia is required. This must be followed by adequate exercises.

Rupture of the *extensor pollicis longus* tendon may occur three weeks after injury or later as a result of attrition of the tendon at the site of fracture. Treatment consists of repair of the tendon or transplantation of a neighbouring extensor tendon to the distal segment of the ruptured tendon.

Malunited Colles's fracture may be corrected by manipulation aided by a Thomas's wrench if union is incomplete. When solid bony union has occurred osteotomy of the radius may be required and even a bone graft may be necessary to fill the gap thus produced. However, one sees many cases of grossly malunited Colles's fracture in which function is excellent and the patients are free of symptoms.

A. R. HAMILTON,
Sydney.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

TO THE SUBSCRIBERS OF THE SYDNEY INFIRMARY.[1]

[*Sydney Morning Herald*, June 1, 1850.]

Ladies & Gentlemen. A vacancy occurring in your institution, from the lamented decease of one of your medical officers, I do myself the honor of applying for the office. Having on a previous occasion submitted to you my testimonials of qualification, I feel there is no necessity of again troubling you with a perusal of them: I may remind you that, though a native of this Country, I was educated in some of the first medical schools in Europe, and received upon my examination at the Royal College of Surgeons of London "in company with my late esteemed friend Dr. HOBSON of Port Phillip" a certificate of honour of having distinguished myself in my examination, from the then President of the Examining Board the late Sir Anthony Carlisle.

I am not seeking the situation from a pecuniary view, but from the principle that, where the native born of the colony possess competency, they have a prerogative in filling the different offices in their home institutions: combined with the fact, that a greater degree of usefulness and professional knowledge is attained by attendance upon the indigent sick than upon other classes of the community.

Assuring you of my desire to promote the interests of your valuable institution,

I beg to remain Ladies & Gentlemen
Your most obedient servant
R. M. Cartwright M.R.C.S.L., &c.

53 Pitt St 31 May 1850.

Correspondence.

EWING HOUSE: ORAL DAY SCHOOL FOR DEAF CHILDREN.

SIR: We feel it might be of some interest to members of the profession in Victoria to know that the clinic attached to the above school, at the request of members of the medical profession in Melbourne and Ballarat, has been testing children suspected of deafness. We are able to test children from the age of three months at Ewing House. The methods used for these tests are the same as those used in leading research centres overseas and our staff is trained at the Manchester University Clinic.

The school and clinic were established at the suggestion of Professor Ewing and Dr. Ewing, of the Manchester University, during their visit to this country in 1951 and have been organized and set up under their guidance.

It may not be generally realized that in England children are automatically referred for hearing tests in the following circumstances: (*a*) Family history of congenital deafness. (*b*) Pre-natal rubella. (*c*) Post-meningitis. (*d*) Post-measles (before twelve months). (*e*) Where a child is to be adopted by foster parents.

It has been found, at the Manchester Clinic, that to ensure oral success, the special education of the deaf should begin as soon as deafness has been discerned, if possible before the age of twelve months. At this age, the child's voice is still normal; whereas at two and a half years, in the absence of special help, he is usually silent and the most vital period of educational opportunity has been missed.

At the above clinic we like to see the very young child two or three times a week, for the first month at least. If the child is found to have a hearing loss, parents may then enrol for monthly visits for parent guidance and an education programme. There is no charge for these services. We would be happy to supply further information if it is required.

[1] From the original in the Mitchell Library, Sydney.

We are constantly encountering children who are referred to the clinic too late for them to derive full benefit from their special education. We would therefore greatly appreciate your help in publishing this letter in THE MEDICAL JOURNAL OF AUSTRALIA for the information of Victorian members.

Yours, etc.,

NANCY S. JOHN,
President, Victorian Committee for the Promotion of Oral Education of the Deaf.

1448 Gregory Street,
Ballarat,
Victoria.
November 14, 1952.

THE AUSTRALIAN ABORIGINAL AND OURSELVES.

SIR: Your editorial in the issue of November 1, 1952, on the "Australian Aboriginal and Ourselves" is most apt. You say: "It may be asked just what place this discussion has in a medical journal . . ." All your readers will readily answer that inquiry. Anthropology has a ready place in a scientific journal. Here we have a dying race on our hands—a race misunderstood and unwanted. Their deaths have been well-nigh a biological necessity, in the sense that a more powerful and voracious animal will quickly root out its weaker and simpler competitors for the same prize. The prize is Australia. Civilization in all its arrogance has submerged the aboriginal, till in absolute silence, he is now relegated to aboriginal stations and a large aboriginal reserve in Northern Australia. Yes, sir, he is relegated to such. In Queensland (and till recently in Federal territories) he is without a vote, not entitled to own property, not permitted to spend his wages as he wishes, and not allowed to live where he wishes. He is deprived of so many human rights that clearly his governors do not regard him as a human being, with democratic human rights. He is regarded as a child with only the right to live.

Here we see the "monstrous fiction of racial superiority" endowed with executive approval. Sir, as aboriginal adult human beings in most if not all Australian States are being so treated, you will readily concede these words have a right to appear in your journal as a logical sequence to your editorial. Of course, special permission is granted certain aboriginals with special talents to live normal lives—always with submission to their protectors.

Because our motives for our depriving the aboriginal of his human rights are considered kind and protective, few people are worried about this frightful situation. Even those anthropological associations whose prime function is the care of the aboriginal are not worried about his slave position in our States.

Sir, the granting of full civic rights to all aborigines is an utter necessity if we are sincere in our protestations of adherence to democratic ideals. At least each aboriginal ought to be asked if he wishes to be free or enslaved. Paragraph 29 of Magna Charta (1297) surely applies to this sad people. Today more than ever Magna Charta and its principles are cherished by free peoples, scientists and especially by us doctors—who flourish best in a free atmosphere. The objection that free natives would drink, gamble or otherwise squander their freedom comes from quarters apparently oblivious of the white man's similar and frequently witnessed tendencies. Actually we at present are protecting our aborigines in a similar but more kindly fashion than is witnessed in some protective manœuvres abroad, but good motives do not excuse the filching of the liberties of any people. Our medical confreres might well follow your lead, sir, in regarding aborigines as our equals and not as our biological, social or evolutionary inferiors.

Yours, etc.,

JOHN R. S. LAHZ.

Ballow Chambers,
Wickham Terrace,
Brisbane.
November 18, 1952.

DANGERS OF MARKING INK TO BABIES.

SIR: Methæmoglobinæmia as a result of poisoning by certain aniline dye substances has been reported in your journal (McDonald, THE MEDICAL JOURNAL OF AUSTRALIA, January 27, 1951). A recent occurrence amongst babies born in this hospital is worth recording as it illustrates a method of absorption of aniline that may not be generally known.

As a method of dealing with the gross overcrowding in this hospital, the Hospital and Charities Commission of Victoria has made available 30 beds in small suburban private hospitals for the post-natal care of mothers and babies after normal delivery. The usual procedure is that the mother and baby are transferred two days after confinement. In one such private hospital there were eleven mothers and babies varying from three to eleven days old. One morning a batch of new napkins was marked in this suburban hospital with one of the popular brands of marking ink, and before washing these napkins were pinned on the babies. Two hours later one baby became cyanosed, and the sister in charge of the babies promptly administered oxygen, but noted that there was no improvement in colour. Shortly afterwards six more babies became cyanosed. They were rapidly transferred to the Children's, Queen Victoria and Women's Hospitals, where the diagnosis of methæmoglobinæmia was made. Marking ink was obviously present on the skins of these babies where the napkin had made contact. Appropriate intravenous methylene blue was given, and all the babies made a rapid recovery.

This incident illustrates the fact that sufficient dye may be absorbed through the skin to cause severe methæmoglobinæmia. It also illustrates the dangers of using dyed fabrics on babies before the dye is adequately fixed in the fabric by drying and washing.

Yours, etc.,

J. C. LAVER,
Medical Superintendent.

The Women's Hospital,
720 Swanston Street,
Carlton,
Victoria.
November 20, 1952.

ALOPECIA AREATA.

SIR: Not being a dermatologist nor an endocrinologist, my knowledge of the ætiology and treatment of *alopecia areata* is limited. I have observed cases of the disease progress to complete baldness. I have at present under my care a case in which dramatic improvement has followed the use of a pituitary extract given by injection. I am aware that patients recover at times without treatment. I have recorded my observations in a short article, and I will be grateful if any dermatologists or other medical men can throw any further light on the problem from their own observations.

Yours, etc.,

S. J. CANTOR.

Sunbury,
Victoria,
November 25, 1952.

Naval, Military and Air Force.

APPOINTMENTS.

ROYAL AUSTRALIAN AIR FORCE.

THE following information is published at the request of the Director-General of Medical Services, Royal Australian Air Force.

The undermentioned medical officers of the Royal Australian Air Force General Reserve have been appointed to established posts for consultants and specialists for service in a part-time capacity.

Air Force Headquarters—Staff of D.G.M.S.—Consultants.

Aviation Medicine Research.—Wing Commander D. H. LeMessurier, M.B., Ch.B. (Edin.), M.Sc. (282721).

Dermatologist.—Group Captain J. J. W. Flynn, M.C., B.A., M.B., Ch.M. (261268).

Ear, Nose and Throat.—Group Captain N. E. H. Box, M.B., B.S., D.L.O. (Eng.), F.R.C.S. (Edin.), F.R.A.C.S. (251172).

Hygiene and Tropical Medicine.—Group Captain A. H. Baldwin, M.B., B.S., D.P.H., D.T.M. and H. (Eng.), F.R.A.C.P. (264907).

Ophthalmologist.—Group Captain C. G. H. Blakemore, M.B., Ch.M., D.O.M.S. (Lond.), F.R.C.S. (Edin.), F.R.A.C.S. (1180).

Orthopædic Surgeon.—Group Captain C. H. Hembrow, M.B., B.S., F.R.C.S., F.R.A.C.S. (1184).

Physical Medicine.—Wing Commander G. G. Burniston, M.B., B.S. (261263).

Physician.—Group Captain L. E. Hurley, M.D., M.S., F.R.A.C.P. (2075); Group Captain I. G. McLean, M.D., B.S., M.R.C.P. (Lond.), F.R.A.C.P., D.T.M. (Syd.) (251178).

Resuscitation.—Wing Commander I. H. Cuming, M.B., B.S., F.R.A.C.S. (251214).

Surgeon.—Group Captain C. H. C. Searby, B.Sc., M.B., M.S., F.R.C.S., F.R.A.C.S., Q.H.S. (2041); Group Captain I. B. Jose, M.C., M.B., M.S., F.R.C.S. (Eng.), F.R.C.S. (Edin.), F.R.A.C.S. (1851).

Southern Area—Specialists.

Melbourne.

Dermatologist.—Wing Commander B. N. O. Colahan, M.B., B.S. (3225); Squadron Leader J. A. Conquest, M.B., B.S. (267263).

Ear, Nose and Throat.—Wing Commander T. G. Millar, M.B., B.S., F.R.C.S. (Edin.), F.R.A.C.S., D.L.O. (Lond.) (2081); Squadron Leader D. F. O'Brien, M.B., B.S., F.R.C.S. (Edin.), F.R.A.C.S.(L.O.) (253180).

Genito-Urinary.—Wing Commander K. A. McLean, M.C., M.D., B.S. (1698).

Gynæcologist.—Wing Commander W. M. Lemmon, M.D., B.S., D.G.O. (Melb.), M.R.C.O.G. (251284).

Neurologist.—Wing Commander L. B. Cox, M.D., B.S., M.R.C.P. (Edin.), F.R.A.C.P. (1179).

Ophthalmologist.—Wing Commander T. a'B. Travers, M.B., B.S., M.R.C.P. (Lond.), D.O.M.S. (Lond.), D.Sc. (Melb.), F.R.A.C.S. (1269); Squadron Leader M. H. M. Ryan, M.B., B.S., M.R.C.S. (Eng.), L.R.C.P. (Lond.), D.O. (Melb.), F.R.C.S. (Eng.), D.O.M.S. (Lond.), F.R.A.C.S., F.A.C.S. (252894); Squadron Leader E. D. E. E. O'Brien, M.B., B.S., D.O.M.S. (Lond.), D.O. (Oxon.) (257096).

Orthopædic Surgeon.—Wing Commander J. G. Brown, M.B., M.S., F.R.C.S. (Eng.), F.R.A.C.S. (251457).

Physician.—Wing Commander G. M. Tallent, M.D., B.S., M.R.C.P. (Lond.), F.R.A.C.P. (257739); Squadron Leader J. F. Hughes, M.D., B.S., M.R.C.P. (Lond.), M.R.A.C.P., D.T.M. (282290); Squadron Leader M. V. Clarke, M.D., B.S., M.R.A.C.P. (253717).

Psychiatrist.—Wing Commander B. J. Mulvany, M.B., B.S., D.P.M. (Melb.) (251258); Squadron Leader D. F. Buckle, M.B., B.S., D.P.M. (R.C.P. and S.) (033452).

Radiologist.—Squadron Leader B. T. Glanville-Hicks, M.B., B.S., D.D.R. (Melb.) (257775); Squadron Leader C. R. Laing, M.B., B.S., D.D.R. (Melb.), M.C.R. (A. and N.Z.) (253407).

Surgeons.—Wing Commander A. J. W. Ahern, M.D., B.S., F.R.C.S. (Eng.), F.R.A.C.S. (251884); Wing Commander S. F. Reid, O.B.E., M.B., M.S., F.R.C.S. (Eng.), F.R.A.C.S. (033451).

Urologist.—Squadron Leader L. J. T. Murphy, M.B., M.S., F.R.A.C.S. (251508).

Adelaide.

Anæsthetist.—Squadron Leader H. E. W. Lyons, M.B., B.S. (282726).

Deputy Principal Medical Officer.—Wing Commander S. M. L. Dunstone, M.B., B.S. (281654).

Dermatologist.—Wing Commander W. C. T. Upton, M.B., Ch.M. (Syd.), M.B., B.S. (Adel.) (3455).

Ear, Nose and Throat.—Wing Commander R. McM. Glynn, M.B., B.S., F.R.C.S. (Edin.), D.O.M.S. (R.C.P. and S.), D.L.O. (R.C.P. and S.), F.R.A.C.S. (1850).

Ophthalmologist.—Wing Commander A. L. Tostevin, M.B., B.S., D.O. (Oxon.), F.R.A.C.S. (1883); Squadron Leader M. C. Moore, M.B., B.S., D.O. (Syd.) (287472).

Orthopædic Surgeon.—Squadron Leader W. J. Betts, M.B., B.S., M.Ch. (Liver.) (287464).

Physician.—Wing Commander R. L. T. Grant, M.B., B.S., M.R.C.P. (Lond.), F.R.A.C.P. (1185).

Psychiatrist.—Wing Commander S. B. Forgan, M.B., B.S., D.P.M. (Syd.) (281237).

Radiologist.—Squadron Leader W. G. Norman, M.B., B.S., D.D.R. (Melb.) (283250).

Surgeon.—Wing Commander O. W. Leitch, M.B., M.S., F.R.A.C.S. (281889).

Tasmania.

Deputy Principal Medical Officer.—Squadron Leader G. A. Robbie, M.D., B.S., M.R.A.C.P. (256865).

Ear, Nose and Throat.—Squadron Leader G. J. Ramsay, M.B., B.S. (265308).

Ophthalmologist.—Squadron Leader J. L. R. Carter, M.B., B.S. (1239).

Physician.—Squadron Leader A. J. M. Dobson, M.B., B.S., M.R.A.C.P. (252289).

Surgeon.—Squadron Leader C. Craig, M.B.E., M.B., B.S., M.D., M.S., F.R.A.C.S. (1849).

Eastern Area—Specialists.

Sydney.

Dermatologist.—Wing Commander A. M. Johnson, M.B., B.S., D.R. (Syd.), D.D.M. (Syd.), M.C.R. (Aust. and N.Z.) (267741).

Ear, Nose and Throat.—Wing Commander H. H. Harrison, M.B., Ch.M., M.S., F.R.C.S. (Edin.), F.R.A.C.S. (7270); Squadron Leader R. G. MacKay, M.B., B.S., D.L.O. (261769).

Neurologist.—Wing Commander S. M. Morson, B.Sc., M.B., M.S. (262063).

Ophthalmologist.—Wing Commander E. V. W. Pockley, M.B., B.S., D.O. (Oxon.), D.O.M.S. (Lond.), F.R.A.C.S. (3752); Squadron Leader W. Deane-Butcher, M.B., B.S., D.O. (Syd.) (261296); Squadron Leader P. A. Rogers, M.B., B.S., D.O. (Syd.) (267886).

Orthopædic Surgeon.—Wing Commander W. N. Little, M.B., Ch.M., M.Ch., Orth. (Liver.) (6410); Wing Commander C. P. Hudson, M.B., B.S., F.R.C.S. (Edin.) (261240).

Physician.—Wing Commander L. R. Flynn, M.B., Ch.M., M.R.A.C.P. (263940); Wing Commander W. A. Seldon, M.B., B.S., M.R.C.P. (Lond.) (261660); Squadron Leader K. S. Harrison, M.B., B.S., M.R.C.P. (Lond.), M.R.A.C.P., D.T.M. (Syd.) (261888).

Plastic Surgeon.—Wing Commander B. W. B. Riley, M.B., Ch.M., F.R.C.S. (Edin.) (264370).

Psychiatrist.—Wing Commander J. A. McGeorge, M.B., Ch.M., D.P.M. (7270).

Radiologist.—Squadron Leader B. E. Frecker, B.Sc., M.B., B.S., M.C.R. (A. and N.Z.), M.F.R. (Lond.) (267894).

Surgeon.—Wing Commander E. F. Langley, M.B., B.S., F.R.C.S. (252868).

Urologist.—Squadron Leader D. C. Trainor, M.B., Ch.M., F.R.C.S. (Edin.) (261653).

Oral Surgeon.—Wing Commander J. S. Baird, B.D.S., D.D.Sc., M.D., B.S. (1481).

Newcastle.

Ear, Nose and Throat.—Squadron Leader A. B. K. Watkins, L.R.C.P. (Lond.), M.B., M.S. (Lond.), F.R.C.S., F.R.A.C.S. (2060).

Ophthalmologist.—Squadron Leader J. W. L. Price, M.B., B.S., D.O.M.S. (Lond.), F.R.A.C.S. (Oph.) (262118).

Physician.—Squadron Leader J. H. B. Brown, O.B.E., M.C., M.B., Ch.M. (1474).

Surgeon.—Squadron Leader A. T. Roberts, M.B., Ch.M., F.R.C.S. (Edin.) (1463).

Brisbane.

Deputy Principal Medical Officer.—Wing Commander C. Roe, M.B., B.S. (011370).

Genito-Urinary.—Wing Commander V. N. B. Willis, M.B., Ch.M. (2872).

Ophthalmologist.—Wing Commander J. B. G. Gibson, M.Sc., M.B., B.S. (277428).

Physician.—Wing Commander L. D. Walters, M.D., B.S., M.R.A.C.P. (277535).

Surgeon.—Wing Commander N. G. Sutton, M.B., Ch.M., F.R.C.S. (Edin.), F.R.A.C.S. (2078); Squadron Leader D. P. Sapsford, M.B., B.S., F.R.C.S. (271742).

Oral Surgeon.—Squadron Leader F. G. Christensen, B.D.Sc. (Q.), L.D.S. (Glas.), B.D.S. (Tor.), R.C.D.S. (Ont.), R.S.P.N.S. (Glas.), H.D.D. (Edin.), R.C.S. (Edin.), S.A.D.S.M. (277341).

Periodontist.—Squadron Leader H. H. M. Finemore, B.D.S. (Syd.), D.M.D. (Harvard) (275918).

Western Area—Specialists.

Perth.

Anæsthetist.—Squadron Leader D. R. C. Wilson, M.B.E., M.B., B.S. (297509).

Dermatologist.—Wing Commander T. C. Anthony, M.B., B.S. (297497).

Ear, Nose and Throat.—Wing Commander N. M. Cuthbert, M.C., M.B., Ch.M., D.L.O. (Lond.), F.R.A.C.S.(L.O.) (1465).

Ophthalmologist.—Wing Commander D. R. Gawler, M.B., B.Ch. (Oxon.) (1183); Squadron Leader K. B. Brown, M.B., B.S., D.O.M.S. (Eng.) (297510).

Oral Surgeon.—Squadron Leader W. A. Harms (2757).

Physician.—Wing Commander H. S. Lucraft, M.D., Ch.B., D.T.M. and H. (Lond.), M.R.C.P. (Lond.), F.R.A.C.P. (6376).

Psychiatrist.—Squadron Leader P. C. C. Tresise, M.B., B.S., D.P.M. (Lond.) (297501).

Radiologist.—Squadron Leader D. E. Copping, M.B., B.S. (291527).

Surgeon.—Wing Commander A. R. Robinson, B.Sc., M.D., M.S., F.R.A.C.S. (263475).

The following appointment is promulgated in the *Commonwealth of Australia Gazette*, Number 77, of November 20, 1952.

NAVAL FORCES OF THE COMMONWEALTH.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Appointment.—Ian Douglas Wilson is appointed Surgeon Lieutenant (on probation), with seniority in rank of 21st May, 1948, dated 8th October, 1952.

HONOURS AND AWARDS.

THE following honours and awards made in connexion with the Australian Military Forces have been promulgated in the *Commonwealth of Australia Gazette*, Number 76, of November 13, 1952.

AUSTRALIAN MILITARY FORCES.

The Australian Efficiency Decoration.

5/32053 Honorary Colonel Frank Kenneth Wallace, O.B.E., Royal Australian Army Medical Corps (now Reserve of Officers).

Lieutenant-Colonel VX81138 James Mayo Buchanan, Royal Australian Army Medical Corps (now Reserve of Officers).

Medical Practice.

POLICE OFFENCES (AMENDMENT) ACT, 1908, AS AMENDED.

THE following amendment to the Police Offences (Amendment) Act, 1908, as amended, which provides for the supply of dangerous drugs to sources outside the Commonwealth and its territories, is published in the New South Wales *Government Gazette*, Number 250, of November 21, 1952.

Chief Secretary's Department, Sydney.

POLICE OFFENCES (AMENDMENT) ACT, 1908.

His Excellency the Governor, with the advice of the Executive Council, has been pleased to amend in the manner set forth hereunder the Regulations under the Police Offences (Amendment) Act, 1908, as amended.

C. A. KELLY, Chief Secretary.

The Regulations are amended by *omitting* Regulation 3 and by *inserting* in lieu thereof the following Regulation:

3. (1) No person shall supply or procure, or offer to supply or procure, any drug unless—

(a) he is the holder of a licence in the form or to the effect of the form set out in Schedule 3 or Schedule 4 to the Regulations; and

(b) he complies with the terms and conditions of the licence; and

(c) the person to whom the drug is supplied or on whose behalf the drug is procured is the holder of a licence or authority under the Regulations or is otherwise authorized by the Regulations to have the drug in his possession.

(2) This Regulation shall not apply—

(a) to a person supplying or procuring, or offering to supply or procure, a drug if such person is acting within the scope of an authority conferred upon him by the Regulations; or

(b) to the supplying of or offering to supply a drug—

(i) to any Authority of the Commonwealth or of any Territory of the Commonwealth, duly constituted in that behalf; or

(ii) to the holder of a licence or authority to have such drug in his possession under the law of any other State of the Commonwealth, or under the law of the Commonwealth or of any Territory of the Commonwealth,

where the person supplying or offering to supply such drug is the holder of a licence in or to the effect of the form set out in Schedule 3 or Schedule 4 to the Regulations; or

(c) to the supplying of or offering to supply a drug by way of export to any person or body located in any country or territory outside the Commonwealth and its Territories where the person supplying or offering to supply such drug is the holder of a licence in or to the effect of the form set out in Schedule 3 or Schedule 4 to the Regulations.

Medical Prizes.

HOWARD W. BLAKESLEE AWARD.

THE Howard W. Blakeslee Award of the American Heart Association, in the amount of $1000, has been established to encourage the best standards of scientific reporting, and will be given annually to the individual whose creative efforts have contributed most toward public understanding of the cardio-vascular diseases in any medium of communication, including newspapers, magazines, books, radio, television or films. Material published or produced during the 1952 calendar year is eligible for consideration. Entries must be postmarked not later than January 15, 1953. The winner will be announced at the annual meeting of the American Heart Association, to be held in April, 1953, in Atlantic City. Entry blanks and further information may be obtained from the Chairman, Managing Committee, Howard W. Blakeslee Award, American Heart Association, 44 East 23rd Street, New York 10, New York, United States of America.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held in the Anatomy Theatre, New Medical School, Frome Road, Adelaide, on October 3, 1952.

Somato-Visceral Interrelationships.

MR. D. I. B. KERR read a paper on somato-visceral interrelationships. He said that much interest had centred around the results of cortical ablation in the so-called rhinencephalon; the present review briefly summarized the results of ablation and stimulation in the true olfactory system, the temporal lobe and the hippocampal-hypothalamic-cingulate cortex circuit. "Sham rage" followed ablation of the amygdala, septal region and ventro-medial hypothalamus in cats (but led to tameness in monkeys). "Obstinate progression" occurred after ablation of the olfactory tubercles and interpeduncular nucleus. Catalepsy followed retromammillary and mid-fornical (including periventricular and intralaminar thalamic regions) lesions. Those could be imitated by bulbocapnine injection. "Akinetic mutism" followed anterior thalamic and periaqueductual grey lesions. Ventral tegmental lesions led to emotional poverty.

The hippocampus on stimulation gave somato-visceral responses of affective states; the fornix was mostly silent. Stimulation of the amygdala, septum, *stria terminalis* and anterior commissure (with their bed nuclei), *striæ medullaris*, habenula and upper Meynert's tract (but not the interpeduncular nucleus) led to somato-visceral reactions of mixed character, suggesting a dual outflow, one inhibitory or facilitatory to both somatic and visceral actions, the other acting in the converse fashion between the two divisions (for example, inhibition of blood pressure, respiration and bladder pressure, but facilitation of somatic action). Stimulation of the anterior part of the thalamus led to an "alerting reaction" even in the absence of cingulate cortex. Fascio-vocal responses followed periaqueductual grey stimulation.

Mr. Kerr said that sleep had been said to follow destruction of the hypothalamic autonomic outflow, and that should be correlated with the sleep following damage to the ascending reticular activitating system. It was concluded that emotional experience and expression might be mediated over a variety of systems.

Renal Lesions in Diabetes Mellitus.

DR. R. T. W. REID, in a paper on renal lesions in *diabetes mellitus*, said that there were four kidney lesions to which the person with *diabetes mellitus* was peculiarly susceptible, and of those, nodular intercapillary glomerulosclerosis was for all practical purposes limited to subjects of *diabetes mellitus*. It represented the most specific histological criterion of the presence of *diabetes mellitus*, but occurred in only approximately 25% of cases of *diabetes mellitus* in which autopsy was performed at the Royal Adelaide Hospital. Arthur Allen's conception of the nodular hyaline material arising from the glomerular capillary basement membrane was now accepted by most students of the condition, although the evidence on which it was based was equivocal.

Dr. Reid went on to say that figures in the literature on the incidence of intercapillary glomerulosclerosis in *diabetes mellitus* ranged from 80% to 20%, the higher figures being due to the inclusion of the non-specific diffuse hyaline lesions of benign nephrosclerosis and glomerulonephritis. Moderate to severe grades of arteriosclerosis of both afferent and efferent glomerular arterioles were found in 70% of cases with the nodular lesion, and although no subject was found without significant arteriosclerosis of the afferent arteriole, one did not have efferent arteriolar sclerosis. Five subjects of *diabetes mellitus* who had died in uræmia had an exudative glomerular lesion associated with gross glomerular hyalinization and renal artery atheroma as described by Hall (1952).

Rubella and Pregnancy.

DR. D. PACKER presented some preliminary results of histological studies on the rubella-affected fœtus, dealing particularly with the eye.

DR. J. BONNIN reported on the successful immunization of a series of 120 pregnant women against rubella.

Obituary.

GILBERT WILLIAM BARKER.

DR. G. W. BARKER, who died in September after a long illness, was for over thirty years an outstanding figure in Western Australian medicine. Educated at Wesley College, Melbourne, and the University of Melbourne, he played league football for Fitzroy at the age of seventeen years, and was a tower of strength in the university team at eighteen years. Qualifying in 1908, he served as a house surgeon at the Perth Hospital, and then for several years was engaged in general practice at the mill town of Dwellingup. He was recalled to the Perth Hospital as chief resident medical officer in 1916, and during the difficult war years he demonstrated administrative ability above the ordinary and that almost ferocious energy which characterized his whole life.

On commencing general practice in Perth in 1921, he was immediately appointed district medical officer and police surgeon, and joined the honorary staff of his old hospital as a gynæcologist. With his wide clinical experience and a profound knowledge of both medicine and surgery, he was splendidly equipped for his real life's work, and a large practice quickly followed. He served for many years as the

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 8, 1952.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	5(3)	..	..	1(1)	..	..	..	6
Amœbiasis	..	2	1	..	..	..	..	..	3
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	3(1)	..	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	2(2)	..	20(15)	..	..	..	1	..	23
Diphtheria	1(1)	1(1)	2(1)	..	2(2)	..	..	..	6
Dysentery (Bacillary)	..	..	3(3)	..	2(2)	..	..	..	5
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1(1)	..	..	..	..	..	..	1
Infective Hepatitis	..	17(4)	..	..	6(5)	..	..	..	23
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	3(1)	4	..	..	..	..	..	..	7
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	13(7)	4(2)	3	8(7)	..	4(1)	..	..	32
Puerperal Fever	..	1	3(2)	..	..	..	..	..	4
Rubella	..	171(116)	3(2)	..	2(2)	..	..	3	179
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	9(6)	29(21)	..	4(2)	4(3)	..	..	..	46
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	2(1)	..	..	..	..	..	2
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	20(16)	12(7)	23(16)	6(4)	16(8)	5(2)	..	2	84
Typhoid Fever	2	..	..	..	..	..	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	3	..	..	..	..	..	3
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

staff representative on the Perth Hospital Board, as a member of the State Medical Board, as a member of the first Workers' Compensation Board, and as a visiting physician to the Home of Peace. He was elected a Fellow of the College of Surgeons of Australasia on September 7, 1929. As the years advanced, so his practice grew, and no ordinary man could have endured the prodigious demands that were made on his professional life. In the late 1930's his health was not good, and a serious car accident left its mark. When he resigned from the staff of the Perth Hospital in 1941, he immediately answered the call of the Children's Hospital, where a depleted surgical staff were carrying on under great difficulties. Fate dealt a further blow in 1943, when his son John was shot down over France. He carried on valiantly, and it was a great joy to him when he was joined in practice by his son Bill. He was an invalid for the last few years of his life, and in 1951 his wife, who had sustained and encouraged him through the long years, suddenly passed away.

Gill Barker possessed all the finer qualities of the ideal physician. As a physician, as a surgeon, as an obstetrician, his services were eagerly sought. He had a sympathetic and reassuring manner, which inspired confidence, and his skill and wisdom were nurtured by experience, uprightness and integrity. A strict disciplinarian, he was solicitous always for the welfare of the nurses and the house surgeons. The path of the young struggling practitioner was made easier by his patience and guidance. When the going became rough men naturally gravitated to "G.W.B.".

He could have specialized early, but the life did not appeal. His contribution to the good name of the profession was very great. Those who loved and respected him—and there are many—in all schools of opinion, in all ranks and walks of life, when they think of him will say to themselves:

> This is the happy Warrior; this is He
> That every Man in arms should wish to be.

CHRISTOPHER BOLLEN.

THE following appreciation of the late Dr. Christopher Bollen has been sent by Dr. A. Sandison.

Dr. Chris. Bollen, of Fitzroy Terrace, Prospect, who died recently, was probably the oldest practising physician in Australia. Born at Mount Barker on July 29, 1866, he was educated at Prince Alfred College and graduated as M.B. at the University of Toronto, Canada, in May, 1888, when he returned to Adelaide at the early age of twenty-one years. Three years later he gained doctorates of medicine at Toronto and the University of Adelaide. He was commissioned in the Commonwealth Military Forces in 1909, and served with the first Australian Imperial Force in command of the South Australian section of the Eighth Field Ambulance in Egypt and on the Somme between 1915 and 1916. He was discharged with the rank of lieutenant-colonel. With the exception of his overseas war service he practised continuously as physician and surgeon in Porth Adelaide and Woodville districts for more than sixty-four years. During the past thirty years he also consulted at his rooms on North Terrace. Always a quiet and retiring man, he had few interests outside his profession, and being most kind and conscientious, he attracted patients from far and near. The passing of Dr. Bollen is a great loss to the profession, and he will be sadly missed by his friends.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Post-Graduate Oration, 1953.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that the sixth Post-Graduate Oration will be delivered in the Great Hall of the University of Sydney on the evening of Wednesday, April 29, 1953. The orator, Professor E. Ford, will speak on "The Life and Times of William Redfern". Those wishing to have their names placed on the invitation list are requested to communicate before February 1, 1952, with the Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483.

Medical Appointments.

Dr. C. J. Cummins has been appointed Deputy Director-General of Public Health and Senior Medical Officer of Health for New South Wales.

Dr. G. B. Wilson has been appointed government medical officer at Surat, Queensland.

Dr. G. H. McQueen has been appointed a member of the Central Board of Health, South Australia.

Nominations and Elections.

THE undermentioned has applied for election to the New South Wales Branch of the British Medical Association:

Morris, Marion Erica, M.B., B.S., 1950 (Univ. Sydney), 20 Merlin Street, Roseville.

Diary for the Month.

DEC. 16.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 16.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital: all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.